

COMPARATIVE STUDY OF LIQUID BASED CYTOLOGY AND PAP SMEAR IN CANCER CERVIX SCREENING



Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfilment of the requirements for the award of

M.D. DEGREE (BRANCH-II)

IN

OBSTETRICS & GYNAECOLOGY



APRIL 2013

DECLARATION

I hereby declare that the dissertation entitled “**COMPARATIVE STUDY OF LIQUID BASED CYTOLOGY AND PAP SMEAR IN CANCER CERVIX SCREENING**” is a bonafide research work done by me at **Coimbatore Medical College and Hospital, Coimbatore** during the period from June 2011 - June 2012 under the guidance and supervision of **Dr.MURUGALAKSHMI,M.D.,DGO.**, Assistant Professor, Coimbatore Medical College and Hospital, Coimbatore. This dissertation is submitted to **The Tamilnadu Dr. M.G.R. Medical University**, towards partial fulfilment of the requirement for the award of **M.D Degree (BRANCH-II) in OBSTETRICS & GYNAECOLOGY**

I have not submitted this dissertation on any previous occasion to any University for the award of any Degree.

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetricians and Gynaecologists
ACS	American Cancer Society
AGC	Atypical Glandular Cell
AHRQ	Agency for Health Care Research and Quality
AIS	Adenocarcinoma in situ
ASC	Atypical Squamous Cell
ASC-H	Atypical Squamous Cell –cannot exclude High grade lesion
ASC-US	Atypical Squamous Cell – Undetermined Significance
AUB	Abnormal Uterine Bleeding
CIN	Cervical Intraepithelial Neoplasia
DNA	Deoxy ribonucleic acid
FDA	Food and Drug Administration
HIV	Human Immuno Deficiency Virus
HPV	Human Papilloma Virus
HSIL	High Grade Squamous Intraepithelial lesion
LSIL	Low Grade Squamous Intraepithelial lesion
RCI	Reid Colposcopic Index

Rb	Retinoblastoma gene
SCJ	Squamo Columnar Junction
SCC	Squamous Cell Carcinoma
STD	Sexually Transmitted Disease
TZ	Transformation Zone
US	United States
VIA	Visual Inspection after Acetic acid
VIAM	Visual Inspection after Acetic acid with Magnification
VILI	Visual Inspection after Lugol's Iodine
WHO	World Health Organisation

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Comparative study of Liquid Based Cytology and Pap smear in Cancer cervix screening

ABSTRACT

Objective:

Cervical cancer is a preventable disease. Screening for precancerous lesion of cancer cervix is one of the secondary prevention activities. In 1940's Pap smear was introduced for cancer cervix screening. The imperfect sensitivity and variable smear quality of Conventional Pap collection lead to the development of Liquid Based Cytology (LBC). The aim of this study is to evaluate liquid based cytology and to compare the sensitivity of liquid based cytology with conventional Pap smear.

Methodology:

This study was carried out on 100 randomly selected women of aged 21-60 years who presented with symptoms of vaginal discharge, lower abdomen pain, post coital bleeding, irregular periods and with cervical lesion from the Gynaecology outpatient department at CMCH between June 2011 – June 2012. Specimen was collected for both conventional pap smear and liquid based cytology then colposcopic guided biopsy was performed in all 100 cases. By using biopsy proven CIN cases as the gold standard the sensitivity of both the cytology method was obtained.

Results:

In our study LBC showed abnormality in 32 cases and in Pap smear it was in 17 cases. The rate of Unsatisfactory smear was low in LBC than Pap smear (1% vs 6%). The rate of prediction of infectious agent was more with LBC (14%) than Pap smear (3%). It is noted that Low grade squamous intraepithelial lesion (16%) and High grade squamous intraepithelial lesion (10%) prediction was more with LBC than Pap smear (LSIL 5%, HSIL 1%) and it was statistically significant. The prediction of Atypical Squamous cell (ASC) category was more with Pap smear than LBC (8% vs 2%). The false negative rate of Pap smear was more than LBC (49% vs 3%). The sensitivity for detection of a histologically proven lesion is significantly higher in LBC compared to Conventional Pap smear (96% vs 51%).

Conclusion:

It is inferred from this study on comparing LBC with Conventional Pap smear relative to histology, Liquid Based Cytology is better than Conventional Pap test in detecting preinvasive cervical lesions. Liquid Based Cytology showed increased sensitivity for the prediction of cytologic abnormality and decreased false negative rate compared to Pap tests.

KEY WORDS:Cancer cervix, Liquid Based Cytology, Conventional Pap smear.

INTRODUCTION

Cervical cancer is the most common gynaecologic neoplasm. It is the leading death causing cancer among women of developing country. Recent estimates point out that every year 134420 women are diagnosed with cervical cancer and 72825 die from the disease in India ⁽²⁴⁾. Cervical cancer is an important public health problem because of its high mortality.

Cervical cancer is a preventable disease. Prevention lies mainly in early detection. The risk of cervical cancer is mainly due to persistent HPV infection, older age, and other demographic, behavioural, and medical risk factors, that vary among population worldwide.

Screening is a secondary level of prevention which is done to detect or rule out disorders at an early stage in healthy person. Screening and treatment of Precancerous lesion of cervical cancer is one of the secondary prevention activities.

In 1940s, cervical cancer screening was first made possible by the introduction of the Papanicolaou (Pap) smear. Population – based screening with Pap smear has been used to detect precancerous lesions since 1960 which leads to a decline in the number of invasive cervical cancer and also higher rate of detection of pre invasive lesions of cervix.

The Pap smear technique is simple and inexpensive but the sensitivity of a single Pap test is limited which varies between 50 – 70%. The Pap test has high false–negative rate which is associated with several factors of both sampling and interpretation. Uneven cell distribution, overlapping cells, blood, or inflammation in conventional Pap smear makes its interpretation difficult.

The imperfect sensitivity and variable smear quality of conventional Pap collection have driven the development of Liquid – Based Cytology (LBC) as a substitute to conventional Pap smear.

The most important benefit of LBC consist of, a probable increase in prediction of high – grade cervical intra epithelial neoplasia (CIN), reduction in the number of unsatisfactory smears, most of the collected cellular material is available for laboratory processing, and the residual specimens can be used for HPV DNA testing .

The expenditure of LBC method is significantly more when compared to conventional Pap method. In developing countries where the resources are inadequate the usage of LBC method for cervical cancer screening programs has a particular concern due to its high price. While comparing LBC and Pap method, if considerable improvement in the performance of LBC method is not achieved, its usage for cervical cancer screening program may not be justified.

The aim of this study is evaluation of liquid based cytology and comparison of sensitivity between conventional Pap smear and Liquid Based Cytology. The performance of both techniques were compared and validated by a histological follow up.

Aim of the Study

AIM OF THE STUDY

1. To evaluate Liquid Based Cytology.
2. To compare the sensitivity of Liquid Based Cytology with
Conventional Pap smear.

Materials and Methods

MATERIALS AND METHODS

DESIGN OF THE STUDY

Prospective randomised evaluation of diagnostic tests

METHODOLOGY AND TECHNIQUES

Sample size – 100 subjects

Subjects are randomly selected from the out patients attending the Gynaecology department of Coimbatore Medical College Hospital between June 2011 and June 2012.

Inclusion criteria

Women aged 21 to 60 years presenting with complaints of abnormal vaginal discharge, irregular periods, lower abdomen pain, post coital bleeding, or abnormal cervical findings on per speculum examination were studied randomly.

Exclusion criteria

Women aged less than 21 years, pregnant women, women who underwent hysterectomy or prior treatment for CIN, and proved cancer cervix cases.

After a detailed history and getting informed consent, thorough clinical examination was done, specimen was collected for cytology, and colposcopic guided biopsy was performed in all 100 cases.

LABORATORY TESTING

By putting the patient in dorsal position, per speculum examination was done, after visualisation of the cervix. Conventional Pap smear was collected by using the Ayer's spatula and the cells were smeared on the glass slide. The glass slide was fixed immediately with 1:1 mixture of 95% ethyl alcohol and ether, and then the slide was sent to the laboratory for processing, where the smear was stained with papanicolaou stain and was reported.

Then another cervical sample was taken with a cytobrush .The head of the brush was detached and placed into the liquid – Prep collection vial which was capped, labelled, and sent to the laboratory for processing and analysis. In the lab the specimen was mixed well using a vortex for 5 to 20 seconds and the entire contents were poured into a clean 15 ml centrifuge tube and it was centrifuged for 10 minutes at 1500 RPM. After centrifugation supernatant fluid was discarded and to the residual pellet cellular base (this component is for encapsulation and adherence of processed cells on a clean glass slide) was added .The specimen was mixed using vortex and pipette 50micro litre onto glass slide. The slide was allowed to dry, stained and was analysed.

In Liquid prep slide the cells are distributed over a small circular area which is 13 mm. In Pap method, as the smear is manually prepared, the thickness of the smear varies. In LBC method, debris, mucus, blood and cell overlap are largely eliminated. The infectious organisms are clearly visible, and air – drying artefacts are not seen. The number of leucocytes is low in LBC method. Hence the epithelial cells and the abnormal cells are easily visualised.

After collecting cytology specimens, colposcopic guided biopsy was performed in all women.

COLPOSCOPY

Colposcopy is an outpatient procedure. It allows examination of the lower genital tract with a microscope. The colposcope consists of a stereoscopic viewing system with magnification settings ranging from 3 to 40 fold attached to a freely movable stand. A high –intensity halogen light provides illumination. Use of a green (red- free) light filter emphasizes contrast by causing the colour red to appear black aiding the examination of vascular patterns.

Steps of Colposcopic examination

Patient was put in dorsal or lithotomy position. Colposcopy was placed one foot from vulva. Cervix was visualised by inserting a Bivalve speculum and colposcope was focused on the cervix. Cervix was cleaned with saline to remove the mucous, 3% acetic acid and lugol's iodine were applied one after

the other, and findings were noted. After documentation of colposcopic findings punch biopsies were obtained from acetowhite and iodine negative areas. When there was no abnormality, cervical biopsy was taken from the anterior cervical lip close to the squamocolumnar junction.

Cytology reporting

Reporting of cytology examination in our study was done using the Bethesda System's 2001 modification. The abnormality in cytology specimen is due to infection, inflammation, reparative changes, and epithelial cell abnormality. The epithelial cell abnormality includes low -grade (LSIL) squamous intra epithelial lesion, high- grade (HSIL) squamous intraepithelial lesion, and atypical squamous intraepithelial lesion.

All cytology specimens were classified either as satisfactory or unsatisfactory. Unsatisfactory specimen was due to scanty cells, improper fixation of slide, debris, mucus, blood cells, inflammation, and other factors which obscure 75% or more of epithelial cells. The specimen was considered to be satisfactory if they contain 5000-10000 well preserved and well visualised squamous cells along with cells from transformation zone.

For the purpose of tabulation, cases whose smears showed infective organisms and all unsatisfactory smears in both cytology methods were considered as cases with normal reports.

In our study cervical biopsy reporting was given using the CIN terms. By using biopsy proven CIN as the “gold standard”, the sensitivity of both the cytology methods were obtained. The cut off points used for the cytology results were ASC-US or higher and for the histology CIN1 or higher.

Review of Literature

REVIEW OF LITERATURE

CRITERIA FOR SCREENING OF DISEASE ⁽¹⁾

The disease to be screened should fulfil the following criteria before it is considered suitable for screening:

- The disease should be an important health problem.
- The disease should have a latent asymptomatic stage.
- There is a test that can detect the disease prior to its onset.
- Facilities should be available for confirmation of the diagnosis.
- There is good evidence that early detection and treatment reduces morbidity and mortality.

Cervical cancer screening matches these criteria quite well.

Compelling Reasons for Cervical Cancer Screening

Cervical cancer is the most common malignancy worldwide. Its high mortality makes cervical cancer an important public health problem. Early detection of cervical cellular changes and Cervical Intraepithelial Neoplasia (CIN) followed by treatment will reduce the risk of developing cancer. Epidemiological data show that organized screening with Pap smear has had a major impact on both morbidity and mortality from cervical cancer ⁽²⁾

Cervical Anatomy

The lower part of uterus is cervix. The lining epithelium of the endocervix is columnar epithelium, and the ectocervix is lined by squamous

epithelium ⁽³⁾. The point where they join is called the Squamo Columnar Junction (SCJ).

The Squamo Columnar Junction

The SCJ is a dynamic point that changes in response to puberty, pregnancy, menopause, and hormonal stimulation. At menarche, the production of estrogen causes the vaginal epithelium to fill with glycogen. Lactobacilli act on the glycogen to lower the pH, stimulating the sub columnar reserve cells to undergo metaplasia ⁽³⁾.

Squamous metaplasia is a normal process and occurs adjacent to the original SCJ, creating a zone of metaplastic epithelium termed the Transformation zone (TZ). It extends from the original SCJ to the physiologically active SCJ. Gland openings and nabothian cysts mark the original SCJ. Nearly all cervical neoplasia, develops within the TZ, usually adjacent to the new SCJ ⁽⁴⁾.

Normal Transformation Zone

The original squamous epithelium of the vagina and ectocervix has four layers - the basal layer, the parabasal layer, intermediate layer and the superficial layer. The superficial layer includes five to eight rows of flattened cells with small nuclei and a cytoplasm filled with glycogen. The nucleus becomes pyknotic, and the cells detach from the surface (exfoliation). These cells form the basis for Papanicolaou (Pap) testing ⁽⁵⁾.

Columnar Epithelium

It has a single layer of columnar cells with mucus at the top and a round nucleus at the base.

Metaplastic Epithelium

Metaplastic cells are normal cells without nuclear atypia. Atypical metaplasia with abnormal nuclear changes is a precursor of dysplasia and malignancy. PH changes, hormonal effect, infection and certain mutagens cause atypical metaplasia ⁽⁶⁾.

Pre invasive cervical cancer or CIN

In 1947 the perception of preinvasive cervical lesion was introduced. The epithelial cell abnormalities which were similar to invasive cervical lesion but restricted to the epithelial cellular layer were identified ⁽⁷⁾.

Cervical dysplasia is a cytological term to describe cells resembling cancer cells. Cervical intraepithelial neoplasia (CIN) refers to the histopathological description in which a part or the full thickness of the stratified squamous epithelium is replaced by cells showing varying degrees of dysplasia, with intact basement membrane ⁽⁶⁾

Dysplasia

▪ Mild dysplasia (CIN-1)

The undifferentiated cells are confined to lower one - third of the epithelium. Mild dysplasia due to infection is often seen in sexually active

young women. CIN-1 is lately described as low grade squamous intraepithelial lesion (LSIL) according to Bethesda classification.

- **Moderate dysplasia (CIN –II)**

The undifferentiated cells occupy lower 50-75% of the epithelial thickness. The cells are mostly intermediate with moderate nuclear enlargement, hyper chromasia, irregular chromatin and multiple nucleations.

- **Severe dysplasia and carcinoma in situ (CIN –III)**

In this grade of dysplasia, the entire thickness of epithelium is replaced by abnormal cells but the basement membrane is intact and there is no stromal infiltration. The cells are mostly parabasal with increased nuclear – cytoplasmic ratio.

CIN II and CIN III are described as high grade squamous intraepithelial lesions (HSIL) according to latest Bethesda classification ⁽⁶⁾.

- **Cancer cervix**

If the dysplastic cells occupy the entire thickness of the epithelium and the basement membrane is not intact, invading the stromal tissues or the adjacent organs, then the disease is called invasive cervical cancer or cervical cancer.

- **Squamous cell carcinoma of cervix (SCC)**

SCC is the most common variety of invasive cancer in the cervix.

Histologically, variants of SCC include large cell keratinizing, large cell nonkeratinizing and small cell types.

- **Adenocarcinoma of cervix**

About 80% of cervical adenocarcinomas are made up of cells of the endocervical type with mucin production.

Aetiology and Pathogenesis

Human Papilloma Virus (HPV)

The most important initiating factor in cervical dysplasia and carcinogenesis is infection with HPV. It infects epithelial cells exclusively; infectiousness depends upon desquamation of infected cells ⁽⁸⁾. HPV infection is sexually transmitted ⁽¹⁰⁾.

There are 14 high risk HPV subtypes; two of the high risk subtypes, 16 and 18, are found in up to 70% of cervical carcinoma ⁽⁹⁾.

Table – 1: HPV prevalence among women ⁽²²⁾

HPV prevalence among women with	Percent
Normal cytology	6
HSIL/CIN2/CIN3	56
LSIL/CIN1	29.4
Cervical cancer	82.5

The mechanism by which HPV affects cellular growth and differentiation is through the interaction of viral E6 and E7 proteins with tumour suppressor

genes p53 and Rb, respectively, resulting in unregulated cellular proliferation⁽¹¹⁾.

Risk factors for Cervical Neoplasia

- Mean age for cervical cancer in the United States is 47 years, cervical cancer peaks at 35 to 39 years and 60 to 64 years of age ⁽⁵⁾.
- Coitus before the age of 18 years
- Multiple sexual partners.
- Delivery of the first baby before the age of 20 years.
- Multiparity
- Poor personal hygiene
- Poor socio economic status.
- Sexual contact with uncircumcised partners as the incidence of HPV is low in circumcised men.
- Smoking and drug abuse.
- Women with STD, HIV infection, herpes simplex virus – 2 infection, HPV infection have a high predisposition to cancer
- Immunosuppressed individuals.
- Women with pre invasive lesions.
- Women who do not come for regular health check-up and Pap tests.

Combined oral contraceptive pills use over 8 year period can cause adenocarcinoma of the endocervix ⁽⁶⁾.

Evaluation⁽⁵⁾

Vaginal bleeding is the most common symptom occurring in patients with cancer cervix. Most often, this is post coital bleeding, but it may occur as irregular or post menopausal bleeding as well. Patients with advanced disease may present with a malodorous vaginal discharge, weight loss, or obstructive uropathy. In asymptomatic women, cervical cancer is most commonly identified through evaluation of abnormal cytologic screening tests.

All women should have a general physical examination including evaluation of the supraclavicular, axillary and inguinofemoral lymph nodes to exclude the presence of metastatic disease. On pelvic examination, cervix and vaginal fornices should be visualised for doubtful areas.

Rectal examination should be done to found out cervical consistency, size, and parametrial extension of disease⁽⁵⁾.

Prevention and Early detection of cancer cervix⁽¹²⁾.

Prevention of cervical cancer consisting of

- Creating awareness about the risk factors among women.
- Promoting practice of safe sex.
- Use of condoms to prevent STDs.
- Life style modification.
- Screening for and early treatment of premalignant lesions
- HPV vaccines.

HPV vaccination

HPV infection is mostly asymptomatic; hence its identification is not easy. HPV vaccination leads to prevention of cervical carcinoma and cervical precursor lesions. Bivalent vaccines against HPV – 16 and 18 and quadrivalent vaccines (HPV-6, 11, 16, 18) have been developed to protect against HPV infection. Duration of efficacy is 3.5- 5 years. Age of administration is between 9-13 years, must be given before the onset of sexual activity. Three doses at 0, 2 and 6 months should be given. Screening with cytology must be continued after vaccination as per schedule ⁽¹²⁾.

Screening for Cervical Intraepithelial Neoplasia

It is technically easy to screen for cervical cancer since.

- The cervix can be easily visualized and tests performed.
- Cervical cancer goes through premalignant changes, and if the diagnosis is made at this stage, cancer can be prevented.
- There is a lag time of 10-20 years before the disease progresses from pre invasive to invasive diseases.

Several screening modalities are available, but cytology is most widely used. In resource – poor settings where cytological screening is not easily available other methods are used ⁽¹²⁾.

Methods used for Cervical Cancer screening ⁽¹²⁾

- Cytology
 - Conventional cytology (Pap smear)

- Liquid – based cytology (LBC)
- Naked eye visual inspection or Down staging
- Visual Inspection after acetic acid (VIA)
- Visual Inspection after acetic acid with magnification (VIAM)
- Visual Inspection after lugols iodine (VILI)
- Cervicography
- HPV DNA testing
- Investigational strategies
 - Polar probe
 - Laser – induced fluorescence

Cervical Cytology

The abnormal cells of cervical neoplasia exfoliate and can be collected by scraping the cervix and staining the smear. The Pap test detects most cervical neoplasia during premalignant phases when treatment outcome is optimized. Pap test was used for cervical cancer screening in the 1950s. Its usage resulted in major decline in the incidence and mortality from cancer cervix ⁽¹⁴⁾. In the developed world cytology based method of cervical cancer screening has been used, which has resulted in the decline of incidence and mortality from cervical cancer ⁽²⁵⁾. In developing countries due to inadequate financial and human resources alternative methods of cervical screening which is more cost effective is being used.

Efficacy of Cytology based Screening

The Pap tests specificity is consistently high, approximating 98 percent. However, estimates of its sensitivity are lower and more variable. A recent meta-analysis found a sensitivity of 51 percent for detection of any grade of CIN by a single Pap test ⁽¹⁵⁾.

Women should be aware of the imperfect sensitivity of the Pap test and the need for periodic screening to compensate.

False negative Pap tests may result from

- Sampling error – in which abnormal cells are not present in the Pap test.
- Screening error – in which the cells are present but missed by the screener.
- Interpretation error – in which abnormal cells are misclassified as benign⁽¹⁶⁾.

Preparation for Cytological Screening

Pap tests should be scheduled to avoid menstruation. Patient should abstain from vaginal intercourse, douching, and medicinal or contraceptive cream preparation for a minimum of 24 to 48 hours before a test. Treatment of cervicitis or vaginitis prior to Pap testing is optimal.

Complete clinical information includes documenting the date of last menstrual period or pregnancy, exogenous hormone use, menopausal status, and past history of abnormal bleeding or abnormal Pap test results, dysplasia or cancer.

Intra uterine devices can cause reactive cellular changes and their use should be noted. Adequate visualization of the cervix is essential for detection of gross lesions and identification of the SCJ.

Sampling of the transformation zone is paramount to the sensitivity of the Pap test ⁽¹⁶⁾.

Methods of Cytological screening

➤ Conventional cytology (Pap smear)

The cervix is visualized after placing a bivalve speculum, and the ectocervix is scraped using an Ayer's spatula and endocervix with a cytobrush. The cells are smeared on a glass slide and fixed in a 1:1 mixture of 95% ethanol and ether.

They are stained using papanicolaou's stain and examined.

Efficacy of Pap smear

The Pap smear has been found to have a poor sensitivity and high false negative rate though the specificity of the test is high ⁽¹²⁾. The main drawback of Pap smear was inadequate shift of cells from the collecting device to the slide, obscuring blood, mucus and variable thickness of smear. The occurrence of false-negative and unsatisfactory Pap smear has prompted the development of LBC and automated screening devices ⁽¹⁸⁾.

➤ Liquid – Based Cytology (LBC)

LBC has been developed to address the limitation of Pap smear and represents the first major change in preparation method for cervical screening

samples. The LBC corresponds to a sampling where cells are put in suspension in a liquid transport medium. The cytology specimen is taken either with a cyto brush or by using both the spatula and endocervical brush. The specimen is then rinsed in the bottle containing a fixative fluid, or the tip of the cyto brush is cut and left in the bottle. In LBC the smearing is done in the laboratory and not manually as in Pap smear where the physician prepares the smear. At present, two methods of LBC – Thin Prep and Sure Path, which use automats, were validated by Food and Drug Administration and are, used frequently ⁽¹⁸⁾. Although LBC has been available for less than a decade, researchers estimate that approximately 80% of Pap tests now performed in the United States is LBC.

CURRENT METHODS USING LBC TECHNOLOGY:

- Thin prep
- Sure path (Auto Cyte PREP or CytoRich LBC)

Sure path allows for the use of all three collection devices; the spatula, the broom, and the endocervical brush ⁽¹⁴⁾ but with modified device tips that can be broken off and sent to the laboratory in the liquid medium. The liquid medium is ethanol – based fluid which maintains cell morphology and nuclear features. In the Sure path method the tip of the endocervical brush is cut and put in the collection bottle containing the liquid medium. By doing so all the scraped cervical cells attached to the endocervical brush has been used for processing and smearing. In the laboratory the bottles are

centrifuged, processed with automated Prep stain machine and smears are prepared.

Thin prep requires immediate and vigorous agitation of the chosen collection device in the liquid medium, after which the device is discarded. In this method by means of T₂₀₀₀ or T₃₀₀₀ machine processing of liquid medium is done. The slides are processed independently with the T₂₀₀₀ device whereas with the totally automated T₃₀₀₀ device around 80 slides can be processed in a single rotation. The slides are then stained and microscopically assessed the same way as in Pap method ⁽¹⁷⁾.

In LBC the area of the slide covered with cells are less than with conventional smear. However obscuring blood, mucus, debris and cellular overlap are largely eliminated. The abnormal cells that might be few in number clustered and obscured on a conventional smear will be randomly and evenly distributed over the area of the LBC slide and thus be more visible for detection⁽¹⁶⁾. Thin Prep and AutoCytePrep specimens have been examined independently, from the same specimens, and there was a high degree of concordance between the two techniques ^(23, 24).

Advantages of LBC

- Better sensitivity and specificity in view of the fact that sampling error is reduced.
- Lower rate of unsatisfactory cervical samples.
- Lesser time for interpretation

- HPV DNA testing is done from the remaining liquid medium ⁽¹⁸⁾.
- Enhanced cytoplasmic and nuclear details.

Comparison of LBC & Conventional Pap smear

Liquid based cytology now accounts for most of the Pap test performed in the US. Both LBC products are FDA – approved to claim a 65- percent increased detection rate of HSIL compared to conventional smear

LBC is more sensitive and accurate for the detection of both squamous lesions and adenocarcinomas of the cervix ^(20, 21).

Since 1950 the Pap method is being used for cancer cervix screening. Its usage resulted in decreasing the occurrence of cancer cervix to 79% and death due to cervical cancer was reduced to 70% ⁽⁵⁾. The Agency for Health Care Research And Quality(AHRQ), undertook a literature review of conventional cytology testing techniques and compared them with newer technologies designed to reduce the false-negative rate ⁽²⁶⁾. For this project, five reports were analyzed, and found out that the sensitivity of conventional Pap method in predicting preinvasive lesions was 51%.

The accurateness of cervical cytology evaluation was reviewed in three reports. According to those reports, sensitivity of the Pap method in predicting CIN 2 or higher lesions was between 47% and 62% and the specificity was between 60% and 95 % ^(27, 28, and 29). Previously it had been widely believed that sensitivity of the Pap test was in the 80% range ⁽³¹⁾. Recommendations for Pap test screening was based on this perceived 80% sensitivity. Every year about

30% of fresh carcinoma cervix cases occur in women who underwent screening with Pap method, mainly because of sampling, fixation and interpretation error⁽³⁰⁾.

It is obvious that improvement in the Conventional Pap test techniques necessary. False-negative errors occur in sampling, preparation, and interpretation. Sampling errors occur because a lesion is too small to exfoliate cells or the device used did not pick up the cells and transfer them to the glass slide. Preparation errors may occur because of poor fixation on the glass slide, leading to air – drying and an inability to interpret the results. The slide may also be too thick and obscured by vaginal discharge, blood, or mucus. The thick slide also leads to poor fixation because the fixative does not penetrate the cell sample. Interpretive errors occur when the slide contains diagnostic cells that the screening technician did not identify.

Using a Liquid-Based medium to collect the cytologic sample and preserve the collected cervical cells can alleviate sampling and preparation errors. In LBC the cells are distributed uniformly in a smaller area of the slide.

The AHRQ reported that liquid-based cytology assessment improved the sensitivity of the Pap test to the stated goal of 80%. With this technique, 80% to 90% of cells are transferred to the liquid media, as compared with the only 10%-20% transferred to the slide with conventional cytologic testing. In addition, using liquid-based media eliminates air- drying. The cells are retrieved from the vial by passing the liquid through a filter, which traps the larger

epithelial cells, separating them from the small blood and inflammatory cells. This process leads to a thin layer of diagnostic cells properly preserved and more easily interpreted by the cytologist. This technique reduces by 70% to 90% the rate of unsatisfactory samples encountered with conventional cytologic testing⁽³²⁾.

Down staging

Down staging of cervical cancer is defined as a process of using clinical approaches for early detection of the diseases. In this process, trained paramedical personnel do a speculum examination, identify any visible abnormalities, and refer cases with suspicious appearance to centres with facilities for diagnosis and management. The WHO has introduced down staging for developing countries where screening methods are not universally available⁽¹³⁾. But the sensitivity and specificity of this method is poor⁽³³⁾.

Visual Inspection after Acetic Acid (VIA)

As it is not easy to practise cytology screening tests in a set up with inadequate resources, other methods of screening have been introduced. Acetic acid when applied to the cervix coagulates the mucus and the areas of cells with increased chromatin density. Areas of CIN, neoplasia, HPV- related changes are aceto white. This method has been extensively studied in developing countries and is currently recommended by the WHO as the primary screening test for developing countries. The disadvantage of this test is the high false –positive rate, resulting in large number of referral⁽¹²⁾.

VIA with Magnification

After application of acetic acid, cervix is visualized under magnification using a hand held magnifying lens. Number of false positives can be reduced with this technique.

Visual Inspection after Lugol's Iodine (VILI)

On application of iodine, normal cervical epithelium which is rich in glycogen stains mahogany brown (Schillers test). The abnormal areas, columnar epithelium and areas lined by immature metaplastic epithelium do not contain glycogen and appear mustard yellow. This method has similar advantages and disadvantages as the VIA.

Cervicography

Photograph of the cervix are taken under magnification before and after application of acetic acid and are read by colposcopist.

HPV – DNA Testing

Use of HPV DNA testing for primary screening, instead of Pap smear, is under study. The test is expensive and currently not recommended for routine primary screening in place of cytology. HPV DNA testing is highly sensitive for diagnosis of High grade squamous intraepithelial lesion (HSIL) ⁽¹²⁾.

Polar Probe

The normal and abnormal tissues differ in its tissue impedance to electrical stimulation ⁽¹⁸⁾. Polar probe technique is based on this information.

Laser Induced Fluorescence

It is shown that, the chemical and morphological composition of individual tissues can provoke endogenous tissue fluorescence on low powered illumination. The detection of this spectroscopic difference can be used to differentiate normal and abnormal tissues⁽¹⁸⁾.

Screening Guide Lines

Recommendations for cervical cancer screening are slightly conflicting. The American Cancer Society (ACS) updated recommendations of 2002 states that

- By using Pap method screening is done every year. On using LBC two yearly screening should be done.
- Screening has to be done either at 21 years of age or in 3 years of the beginning of sexual action. At 70 years of age, if the Pap reports were normal for the precedent 10 years screening has to be stopped.
- Screening after hysterectomy for benign disease is not necessary⁽¹⁴⁾.

The American College of Obstetricians and Gynaecologists (ACOG) differs from the ACS recommendations by stating that

- Women younger than the age of 30 should undergo cervical cytology screening yearly and in those older than the age 30 if there is no associated risk factors screening should be done once in 2 to 3 years using either LBC or conventional Pap testing furthermore. According to ACOG, women who are 30 and above ideally should undergo both

cytology and HPV DNA testing. If results are negative using this combination, a woman can be retested at only 3 year intervals ⁽¹⁹⁾

(Table-2). The negative predictive value of this combination test exceeds 99% ⁽⁵⁾. In women younger than 30 years, the high prevalence of high risk HPV infection makes this strategy too nonspecific for use.

Table – 2: Comparison of Cervical Cytology Screening

Guide line	American Cancer Society (ACS)	ACOG
Initial screening	Age 21 or 3 years after sexual activity	Same as ACS
Interval	<ul style="list-style-type: none"> • Every year for conventional Pap • Every 2 years for LBC • Every 2-3 years after age 30 with 3 consecutive normals 	<ul style="list-style-type: none"> • Every year for either LBC or conventional smear • Every 2-3 years after age 30 with 3 consecutive normals
Discontinue	<ul style="list-style-type: none"> • Age 70 if 3 consecutive normals in 10 years 	<ul style="list-style-type: none"> • No upper age limit

Screening guide lines for countries with inadequate resources

The median age of cervical cancer diagnosis is in the mid to late forties approximately a decade later than CIN ⁽¹⁶⁾, carcinoma cervix mostly occurs at the age of 35 to 39 years and 60 to 64 years. Hence in developing countries

where resources are inadequate screening programs should involve women in fourth decade of life.

Pre invasive cervical lesions like CIN predispose to cancer cervix; therefore, compared to frequent screening as per protocol, occasional screening also be able to decrease the prevalence, sufferings and death from carcinoma cervix. Cervical cancer screening done once in 10 years or once in a patient's life time has a major effect in reducing its incidence. Hence screening programmes should focus on screening women of high risk category than on regularity ⁽³⁴⁾. In developing countries, with inadequate funds, the aim of screening should be to include all women of high risk category once in her life time around her 40 years of age ⁽¹³⁾.

REPORTING OF CERVICAL CYTOLOGY TESTING

Bethesda System -2001

In the year 1988, in Bethesda, Maryland, the first National Cancer Institute (NCI) workshop was conducted, where the Bethesda system for the reporting of cytology testing was proposed ⁽⁵⁾. Standardization of cervical cytology reporting took place with the development of the Bethesda system. The terminology was refined in the Bethesda III system 2001. According to this system, potentially premalignant squamous lesion falls into three categories ⁽¹⁶⁾.

- Atypical squamous cells (ASC)
- Low - grade squamous intraepithelial lesion (LSIL)

- High – grade squamous intraepithelial lesion (HSIL)

The ASC category is subdivided into two categories

- those of undetermined significance (ASC-US)
- those in which high-grade lesion must be excluded (ASC-H)

A comparison of the various terms as they relate is shown in Table – 3

The 2001 Bethesda System Cytology Report Components ⁽¹⁶⁾

Specimen type

Conventional Pap test

Thin-layer liquid-based cytology

Specimen adequacy

Satisfactory for evaluation

Unsatisfactory for evaluation

General categorization (optional)

Negative for intraepithelial lesion or malignancy

Epithelial cell abnormality

Other findings that may indicate increased risk

Interpretation of results

Negative for intraepithelial lesion of malignancy

Organisms:

Trichomonas vaginalis

Fungal organisms consistent with Candida species

Shift in flora suggestive of bacterial vaginosis

Cellular change consistent with herpes simplex virus

Bacteria consistent with Actinomyces species

Other non-neoplastic findings (optional)

Reactive cellular changes (inflammation, repair, and radiation)

Glandular cells post hysterectomy

Atrophy

Epithelial cell abnormalities

Squamous cell

Glandular cell

Other:

Endometrial cells in a woman ≥ 40 years of age.

Table –3: Comparison of Cytology Classification System ⁽⁵⁾

Bethesda System	Dysplastic / CIN System	Papanicolaou System
Within normal limits	Normal	I
Infection (organism should be specified)	Inflammatory atypia (organism)	II
Reactive and Reparative changes		
Squamous cell abnormalities		
Atypical squamous cells	Squamous atypia, HPV atypia,	II
1. of undetermined significance (ASC-US)	exclude LSIL, exclude HSIL	
2. exclude high – grade lesions (ASC-H)	HPV atypia	
Low grade Squamous intra epithelial lesion (LSIL)	Mild dysplasia CIN I	
High grade Squamous intraepithelial lesion (HSIL)	Moderate dysplasia CIN 2	III
	severe dysplasia CIN 3	IV
	Carcinoma in situ	
Squamous cell carcinoma	Squamous cell Carcinoma	V

Clinically, the key elements in Bethesda system are assessment of specimen adequacy and epithelial cell abnormality ⁽¹⁶⁾ (Table 4).

Specimen Adequacy

The significant and the quality assurance part of the Bethesda System is its assessment of specimen adequacy. Earlier versions of Bethesda included three categories of adequacy: Satisfactory, Unsatisfactory and a borderline category initially termed “Satisfactory but limited by” in 1991.

The 2001 Bethesda System eliminates the borderline category because of confusion among clinicians as to the appropriate follow-up for such findings and also due to variability in reporting “Satisfactory but limited by” among laboratories. To provide a clearer indication of adequacy, specimens are now designated as “Satisfactory” or “Unsatisfactory”.

The satisfactory smear is one which shows abnormal glandular and epithelial cells. In an adequate Pap specimen at least 8000 to 12000 well-preserved and well visualized squamous epithelial cells should be there. In liquid based preparation 5000 well – visualized /well preserved squamous cells will do. For both conventional smears and liquid based preparations adequacy of Transformation zone part requires a minimum of 10 well-preserved endocervical or squamous metaplastic cells. If more than 75% of squamous cells in the smear is masked by blood and mucus the specimen is labelled as unsatisfactory, as the cells are not identified⁽³⁵⁾.

Table – 4: The 2001 Bethesda System: Epithelial Cell Abnormalities

<p>Squamous cell</p> <ul style="list-style-type: none">▪ Atypical squamous cells (ASC)<ul style="list-style-type: none">○ of undetermined significance (ASC-US)○ cannot exclude HSIL (ASC-H)▪ Low-grade squamous intraepithelial lesion (LSIL)▪ High -grade squamous intraepithelial lesion (HSIL)▪ Squamous cell carcinoma
<p>Glandular cell</p> <ul style="list-style-type: none">▪ Atypical glandular cells (AGC)<ul style="list-style-type: none">○ Endocervical, endometrial, or not otherwise specified▪ Atypical glandular cells, favour neoplastic<ul style="list-style-type: none">○ Endocervical or not otherwise specified▪ Endocervical adenocarcinoma in situ (AIS)<ul style="list-style-type: none">○ Adenocarcinoma

Epithelial cell abnormalities: Significance

A cytology report is a medical consultation that interprets a screening test and is not a diagnosis. Thus a final diagnosis is determined clinically, often with results from histological evaluation ⁽¹⁶⁾.

Atypical Squamous Cells of Undetermined Significance

The most common cytologic abnormality ASC – US precedes the diagnosis of CIN 2 or 3, this risk approximates 5 percent. Three options for evaluation of ASC-US are HPV – DNA testing, colposcopy or repeat cytologies at 6 and 12 months, with referral to colposcopy if either of these is abnormal⁽²⁰⁾. Here cells are found in sheets or singly, nuclei 2 ½ - 3 times the size of an intermediate nucleus with uniform chromatin distribution. The frequency of ASC-US diagnoses should not exceed 2-3- times the rate of SIL⁽³⁵⁾.

Atypical Squamous Cells cannot exclude HSIL

10 percent of ASC is ASC – H. This describes cellular changes that do not fulfil criteria for HSIL cytology, histologic HSIL is found in 25 percent of these cases hence colposcopy is indicated for evaluation⁽²⁰⁾. Atypical squamous cells cannot exclude HSIL includes immature metaplastic cells with increased nucleo cytoplasmic ratios, slight nuclear membrane irregularities and nuclear size variability, suggestive of but not definitive for HSIL⁽³⁵⁾.

Low Grade Squamous Intraepithelial Lesion

This cytology result indicates the likely presence of HPV infection or low-grade neoplasia (CIN I), carries a 15 to 30 percent risk of CIN 2 or 3, LSIL encompasses the cytologic features of HPV infection and CIN I.

Colposcopy is indicated for evaluation. Increased nuclear detail, irregular nuclear membrane, and nuclei 3-4 times the size of intermediate nucleus, sharp irregular cytoplasmic cavitation (HPV effect) are characteristic of LSIL⁽³⁵⁾.

High–grade Squamous Intraepithelial Lesion and Glandular Abnormalities

HSIL, all glandular epithelial cell abnormality and suspicion of carcinoma should be evaluated by colposcopy. HSIL encompasses features of CIN 2 and CIN 3. Management of HSIL includes immediate diagnostic loop excision because colposcopy may miss a high grade lesion. Immature metaplastic type squamous cells showing increased nucleo cytoplasmic ratios (in excess of 50%) nuclear irregularities and coarse chromatin result in a diagnosis of HSIL ⁽³⁵⁾.

Glandular Cell

Squamous neoplasia is the most common diagnosis found upon evaluation of Atypical Glandular Cell (AGC) cytology, but there is also a high risk of both endocervical, endometrial and other reproductive tract cancer ⁽¹⁶⁾.

Non Neoplastic Findings

These findings include *Trichomonas vaginalis*, candida species, *Actinomyces* species, herpes simplex virus, or flora consistent with bacterial vaginosis, and the reactive changes due to inflammation, repair and radiation ⁽¹⁶⁾.

Colposcopy

Colposcopy allows examination of the lower genital tract with a microscope to further evaluate abnormal Pap test results and visible epithelial abnormalities.

COLPOSCOPIC FINDINGS AND TERMINOLOGY

Colposcopically, the squamous epithelium of the cervix appears as a featureless, smooth, pale pink surface. The single cell layer columnar epithelium of the endocervix appears red and velvety due to the proximity of blood vessels.

Adequate visualization of the entire cervical SCJ and upper limits of all lesions defines whether a colposcopic examination is termed satisfactory or unsatisfactory.

Aceto white Epithelium

Epithelium that turns white after application of 3 percent acetic acid is called aceto white epithelium. The components of the cell which contain proteins are coagulated on applying acetic acid and become white. The areas of immature squamous metaplasia, transformation zone, inflammatory, healing, and regenerative epithelium also become acetowhite on applying acetic acid⁽³⁶⁾.

Low grade lesions are thin, less intense, and narrow. The margins are asymmetrical, geographic, fluffy, or angular with fine punctuation or mosaic; occasionally they are separated from the squamo columnar junction; and atypical vessels are not present in low-grade lesions.

In high-grade lesions thick, deep, opaque, grey white, acetowhite areas are present, coarse punctuation or mosaicism are seen in high grade lesions. The borders are regular and well demarcated; both cervical lips are involved in these

lesions. Atypical vessels are seen here. In high-grade lesions, CIN-3 is complex and occupies the cervical os ⁽³⁶⁾.

On applying Lugol's Iodine, normal glycogen rich squamous epithelium and mature metaplastic epithelium present in vagina and cervix take up the iodine and become brown. Dysplastic epitheliums do not have glycogen, and they do not take up iodine and they look mustard or saffron yellow in colour. Based on the colour of the epithelium, normal and abnormal areas in the transformation zone are clearly identified when the aceto white areas are not easily made out ⁽³⁶⁾.

Lesion vascular patterns

The vascular patterns associated with abnormal epithelium include punctuation, mosaicism and atypical vessels.

Fine punctuation and mosaicism, which are created by narrow vessels and uniform intercapillary distances, typify low – grade lesions. A coarse pattern results from wider vessels, variable intercapillary distance, vessel diameter, and spacing. This indicates high grade lesions ⁽¹⁶⁾.

Atypical vascular patterns are characteristic of invasive cervical cancer and include looped vessels, branching vessels, and reticular vessels ⁽⁵⁾.

Several colposcopy grading systems that quantify various colposcopic signs have been developed to improve accuracy. Best known, the Reid Colposcopic Index (RCI) has a reported histologic correlation of 97 percent.

The RCI is based on four colposcopic lesions features ⁽¹⁶⁾. Peripheral margin, color, vascular patterns, and iodine staining. Each category is scored from zero to two and the summation provides a numeric index which correlates with histology.



FIG 1: Slide of Conventional Pap smear (Macroscopic)



FIG 2: Slide of LBC (Macroscopic)

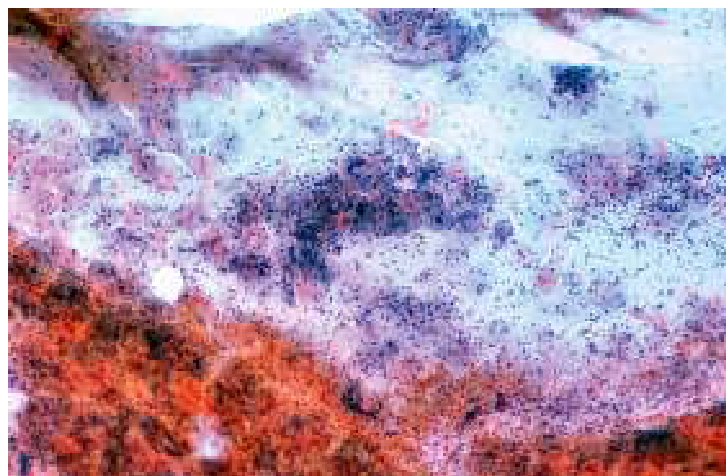


FIG 3: CONVENTIONAL PAP smear

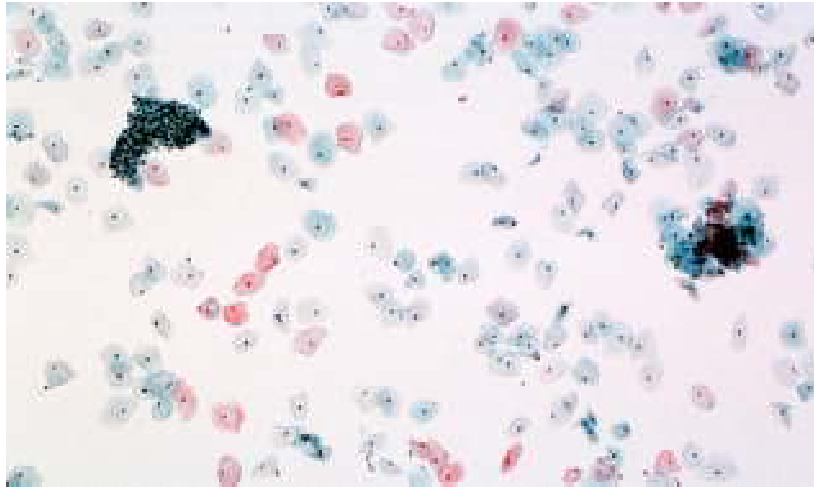


FIG 4: Same Patient - LBC smear

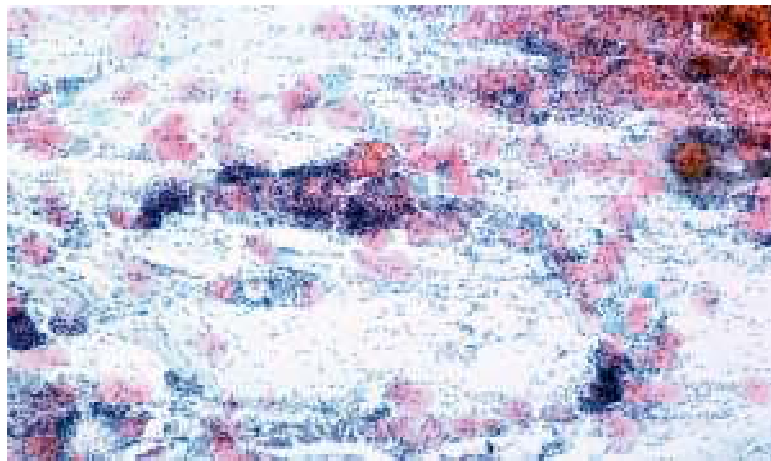


FIG 5: Conventional PAP – Smear Pattern



FIG 6: LBC – Same Patient

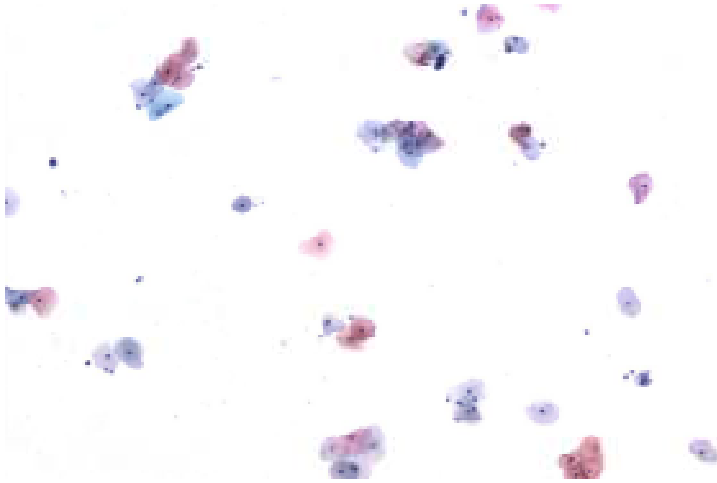


FIG 7: LBC smear - containing 40 squamous cells. Unsatisfactory field



FIG 8: Trichomonas vaginalis in LBC smear



FIG 9: Candida in LBC smear

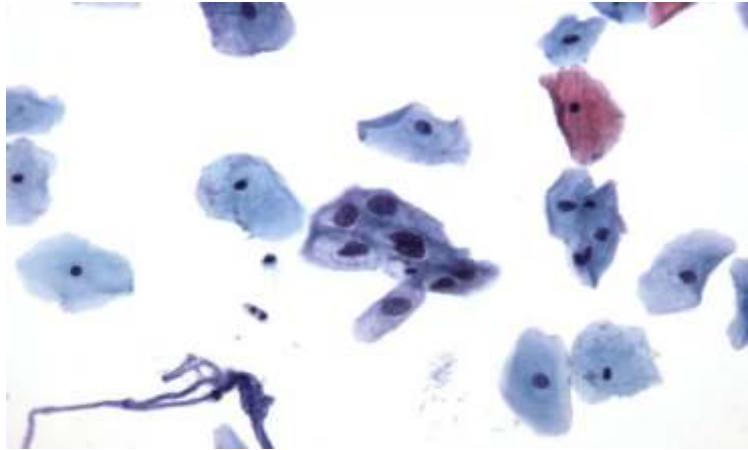


FIG 10: ASC-US in LBC

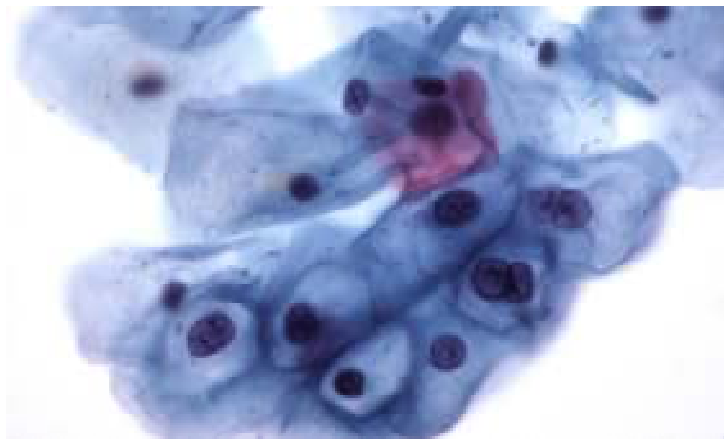


FIG 11: LSIL in LBC

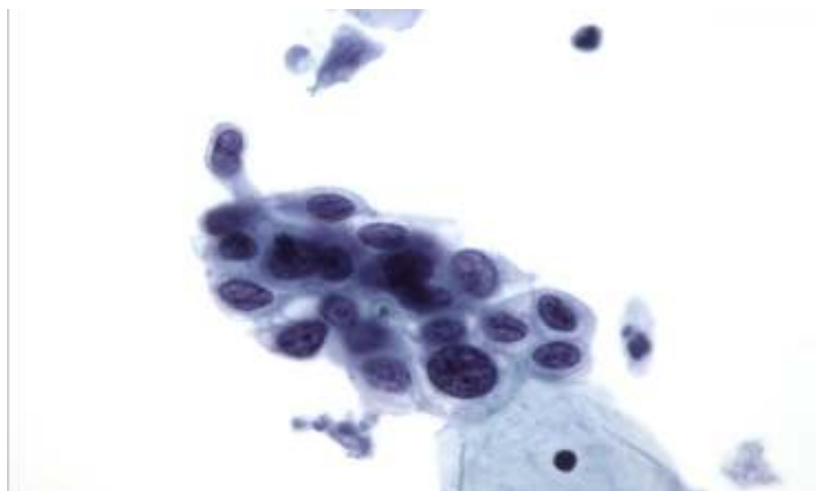


FIG 12: HSIL in LBC

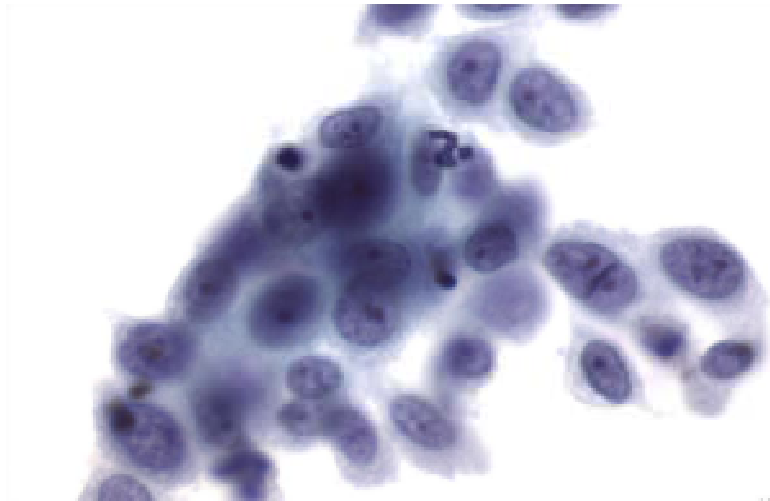


FIG 13: Squamous Cell Carcinoma in LBC



FIG 14: Normal Colposcopic picture

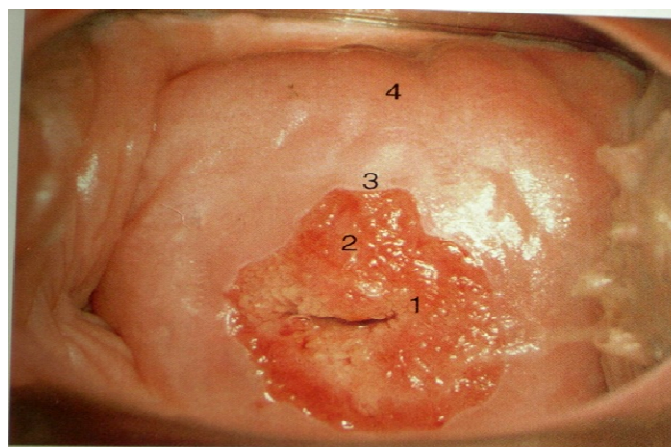


FIG 15: NORMAL COLPOSCOPIC PICTURE showing 1.External os 2.columnar epithelium 3. New SCJ 4.original SCJ



FIG 16: Invasive cancer on colposcopy



FIG 17: Abnormal vascular pattern



FIG 18: LOW GRADE LESION in colposcopy



FIG 19: HIGH GRADE LESION

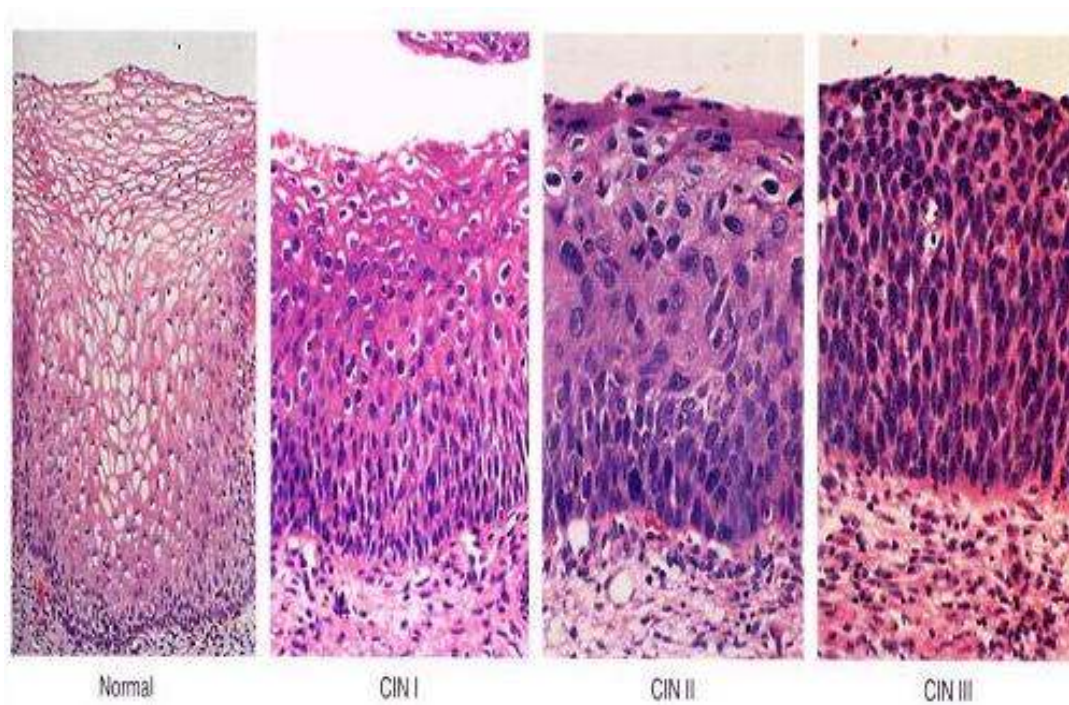


FIG – 20: CERVICAL INTRAEPITHELIAL NEOPLASIA

CIN 1 - Undifferentiated cells occupy lower one third of the epithelium

CIN2 - Undifferentiated cells occupy lower two third of the epithelium

CIN 3 - Undifferentiated cells occupy full thickness of the epithelium.

Results

RESULTS

The present study was carried out on 100 patients who are randomly selected from the Out Patient Department of Gynaecology at CMCH during the period of June 2011 to June 2012. After taking history and clinical examination cytology specimen was collected for both Pap test and Liquid Based Cytology, then colposcopic guided cervical biopsy was taken for all patients.

Table -5: Age wise cases

Age (years)	Cases	Percentage
21 – 30	35	35
31 – 40	40	40
41 – 50	17	17
51 – 60	8	8

It is noted in our study that out of total 100 cases, 35 cases (35%) studied belonged to third decade of life, 40 cases (40%) belonged to fourth decade of life, 17 cases (17%) belonged to fifth decade of life, and 8 cases (8%) belonged to sixth decade of life.

Figure – 21: Age wise cases

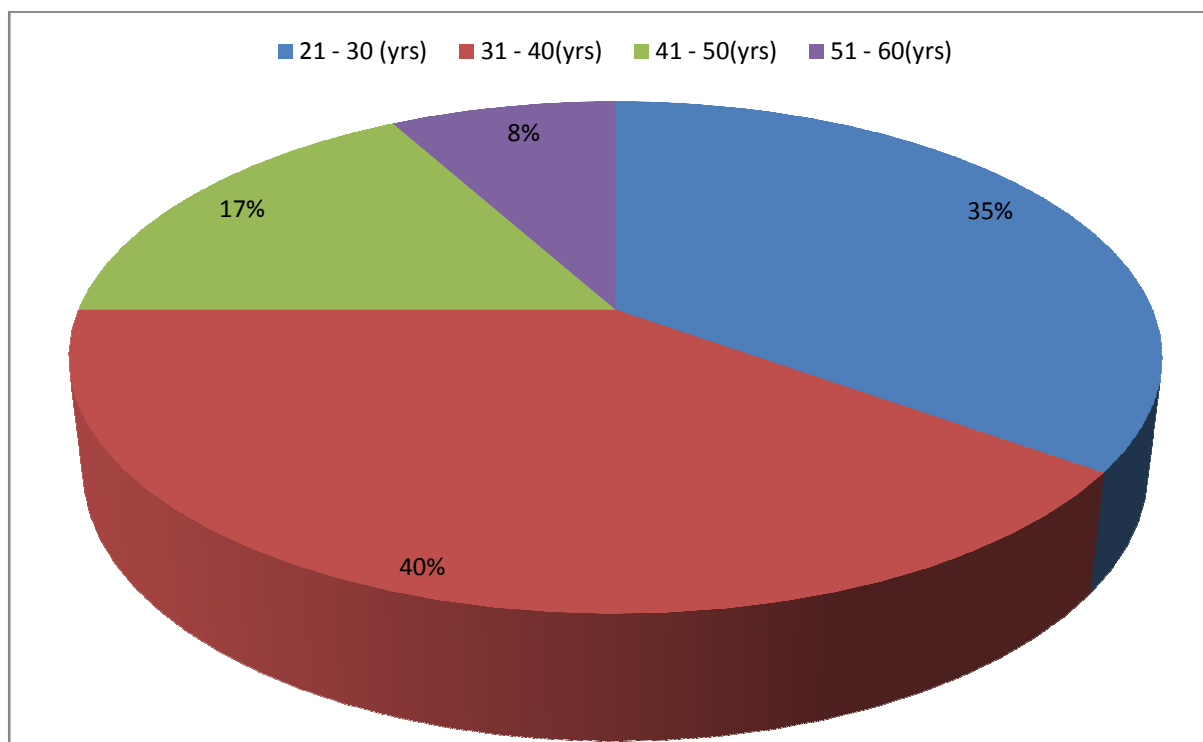


Table – 6: Age wise case distribution

Age(years)	Normal	Abnormal	
		CIN	SCC
21 – 30	31	4	-
31 – 40	26	13	1
41 – 50	8	7	2
51 – 60	2	5	1

In current study , 4 (13%) abnormal cases belonged to third decade of life, 13 (44%) abnormal cases belonged to fourth decade of life, 7 (24%) abnormal cases belonged to fifth decade of life and 5 (17%) abnormal cases belonged to sixth decade of life. Out of 4 squamous cell carcinoma cases, 1 case belonged to fourth decade of life, 2 cases belonged to fifth decade of life, and 1 case belonged to sixth decade of life. In our study 44% of abnormal cases and the earliest age of occurrence of squamous cell carcinoma belonged to fourth decade of life.

Figure-22: Age wise case distribution.

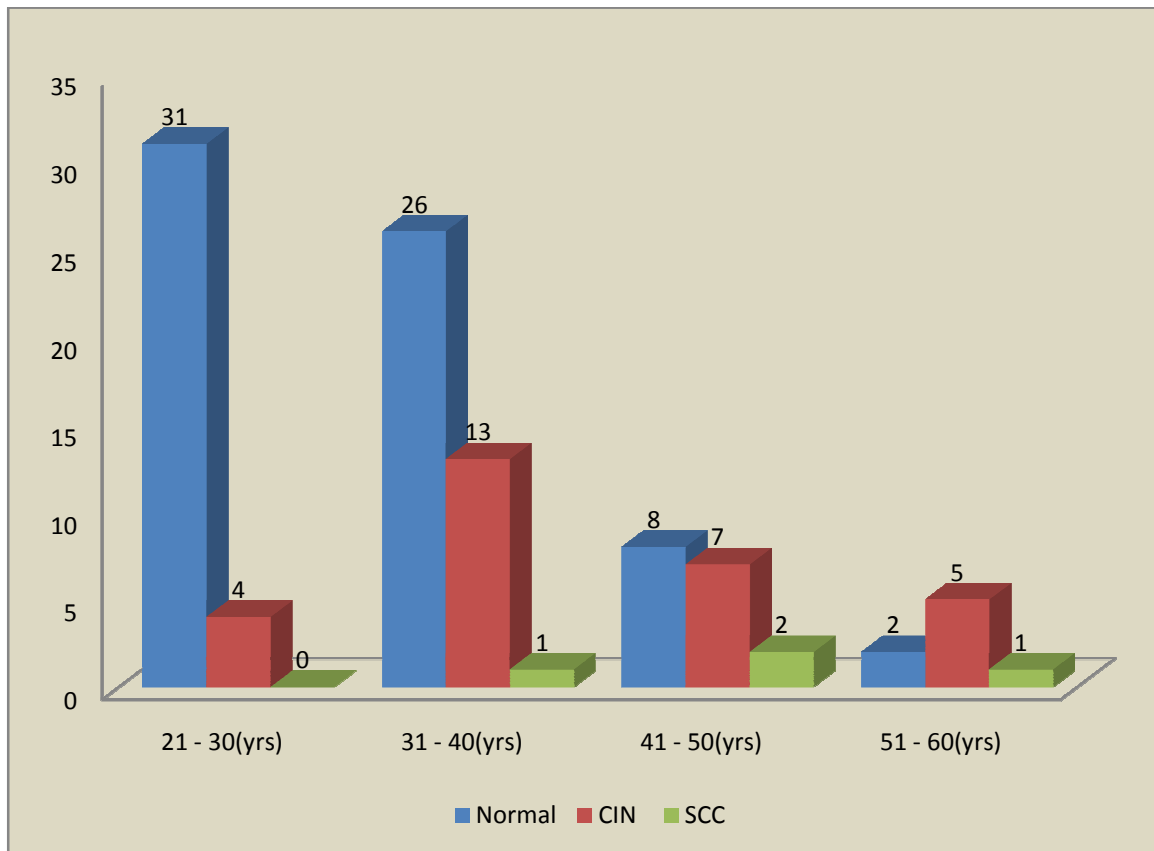


Table-7: Place wise case distribution

Place	Total cases	Normal	Abnormal
Rural	24	18	6
Urban	76	49	27

In the present study out of 100 cases, 24 cases were from rural area and 76 cases were from urban area. Of the abnormal cases 6 cases (18%) belonged to rural area and 27 cases (82%) belonged to urban area.

Table-8: Socio economic class wise case distribution

SE class	Total cases	Normal	Abnormal
I	-	-	-
II	1	1	-
III	29	19	10
IV	70	47	23

It is noted in our study that out of 100 cases, 70 cases belonged to socio economic class IV (Modified Kuppusamy's Scale), 29 cases belonged to socio economic class III, 1 case from socio economic class II.

Of the abnormal cases 10 cases (30%) belonged to socio economic class III and 23 cases (70%) cases belonged to socio economic class IV.

Figure 23: Socio economic class wise case distribution

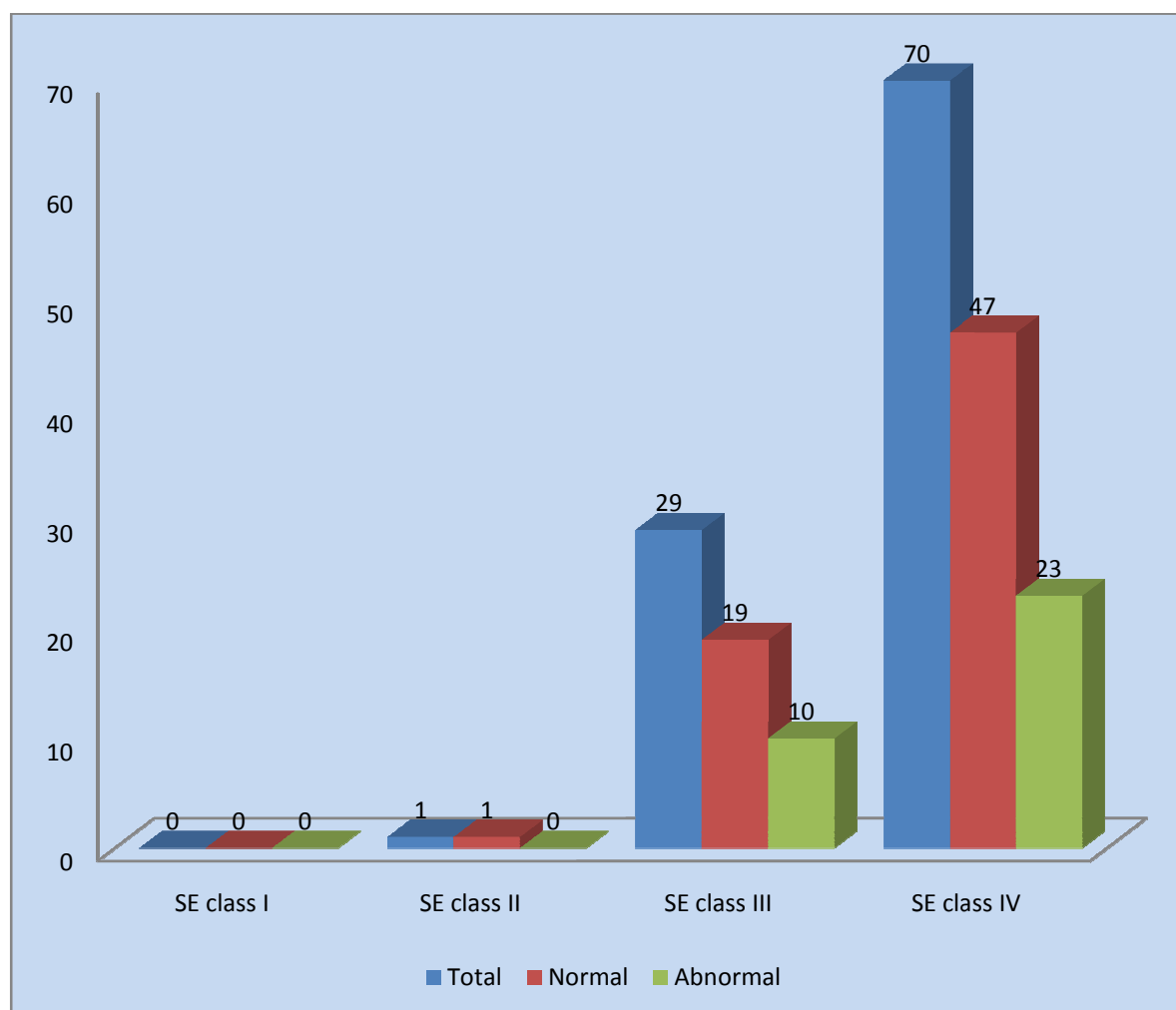


Table-9: Case distribution in relation to age at first coitus

Age at first coitus(years)	Total cases	Normal	Abnormal
Less than 20	48	22	26
21-25	49	42	7
26-30	3	3	-

In our study 48 cases started sexual activity less than 20 years of age,49 cases had first coitus between 21-25 years of age and 3 cases between 26-30 years of age.

Of the abnormal cases 26(78%) cases started sexual activity less than 20 years of age,7cases (22%) started sexual activity between 21-25 years of age and no CIN cases were detected in women who had first coitus between 26-30 years of age.

Figure 24: Case distribution in relation to Age at first coitus

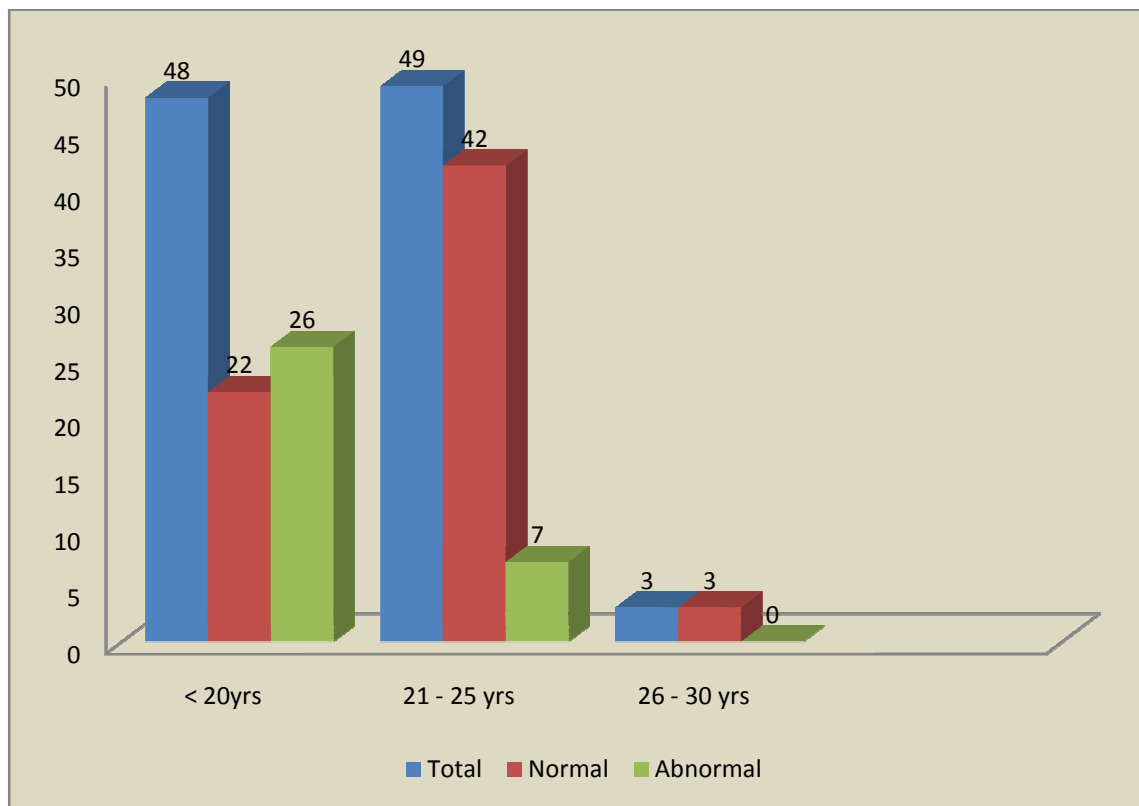


Table-10: Case distribution in relation to Parity index

Obstetric score	Total cases	Normal	Abnormal
Para 1	15	14	1
Para 2	58	47	11
Para 3 & above	27	6	21

In the present study out of 100 cases, 15 cases belonged to Para 1, 58 cases belonged to Para 2 and 27 cases belonged to Para 3 and above.

21 (64%) out of 33 abnormal cases had Para 3 and above, 11 cases (33%) belonged to Para 2, and 1 case (3%) belonged to Para 1.

Figure 25: Case distribution in relation to parity index

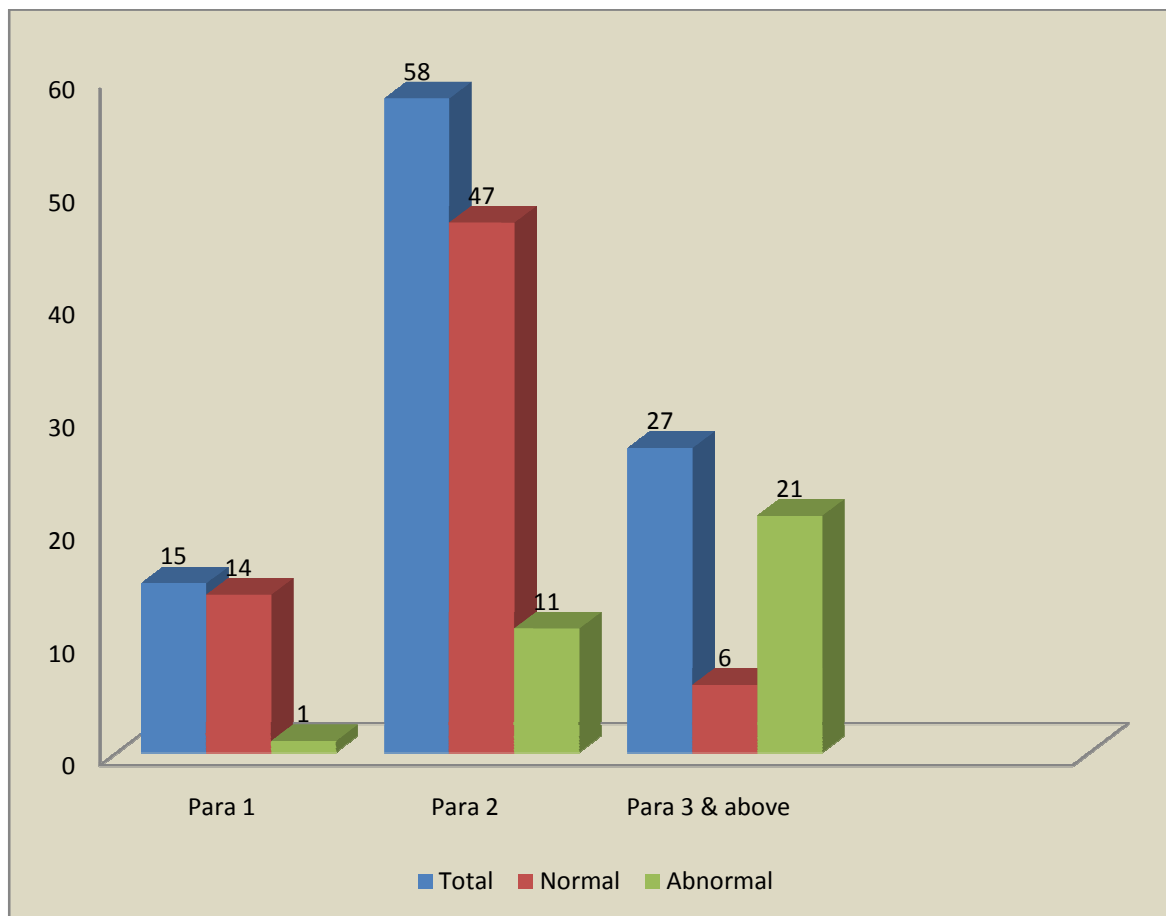


Table-11: Case distribution in relation to presenting symptoms

Symptoms	Total cases	Normal	Abnormal
AUB	6	6	-
Discharge P/V	66	45	21
Lower abdomen pain	20	16	4
Post coital bleed	8	-	8

In our study out of 100 cases, 66 cases presented with symptoms of vaginal discharge, 20 cases with lower abdomen pain, 8 cases with post coital bleed and 6 cases with irregular periods (Abnormal uterine bleeding).

21 (64%) out of 33 abnormal cases presented with discharge P/V, 4 cases (12%) with lower abdomen pain and 8 cases (24%) presented with post coital bleeding. All the cases with post coital bleeding had biopsy abnormality.

Table – 12: Case distribution in relation to clinical findings

P/S findings	Total cases	Normal	Abnormal
Normal	87	67	20
Erosion Cx	3	-	3
Eversion Cx	2	-	2
Hypertrophied Cx	2	-	2
Ulcer Cx	4	-	4
Papillary growth	2	-	2

In current study, 87 cases had clinically normal cervix, 13 cases had lesion on cervix. 20 (61%) out of 87 normal cases and all 13(39%) cases who had clinically detectable lesion on cervix showed HPE abnormality. Of the 13 abnormal cases 3 cases had erosion cervix, 2 had eversion cervix, 2 had hypertrophied cervix, 4 had ulcerative lesion on cervix, and 2 patients had papillary growth on cervix.

Table-13: Case distribution of LBC and Conventional Pap smear

Cytology	Normal	Abnormal
LBC	68	32
PAP	83	17

In our study out of 100 cases, 68 (68%) cases in LBC were normal and 32cases (32%) showed abnormality. In Conventional Pap smear 83 (83%) cases were normal and17 cases (17%) showed abnormality. LBC predicted 15 extra abnormal cases than Pap smear.

Figure 26: Case distribution of LBC and PAP smear

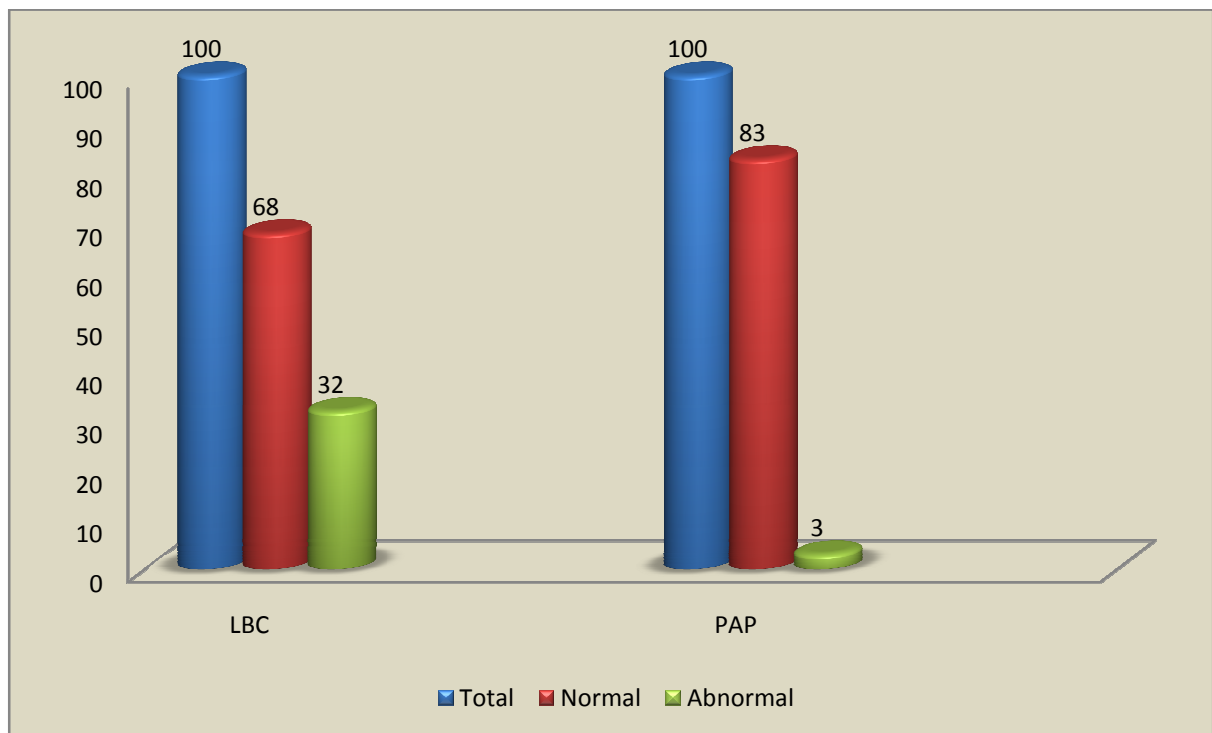


Table-14: Comparison of Specimen adequacy in LBC and PAP

Cytology	Satisfactory smear	Unsatisfactory smear
LBC	99	1
PAP	94	6

In the present study out of 100 cases, 99 smears of LBC were satisfactory for evaluation and 1 smear was unsatisfactory for evaluation. In PAP 94 smears were satisfactory for evaluation and 6 smears were unsatisfactory for evaluation. Unsatisfactory smear in LBC was due to scant cellularity and in Pap smear it is due to thick smear caused by obscuring mucus.

Figure 27: Comparison of Specimen adequacy in LBC and PAP smear

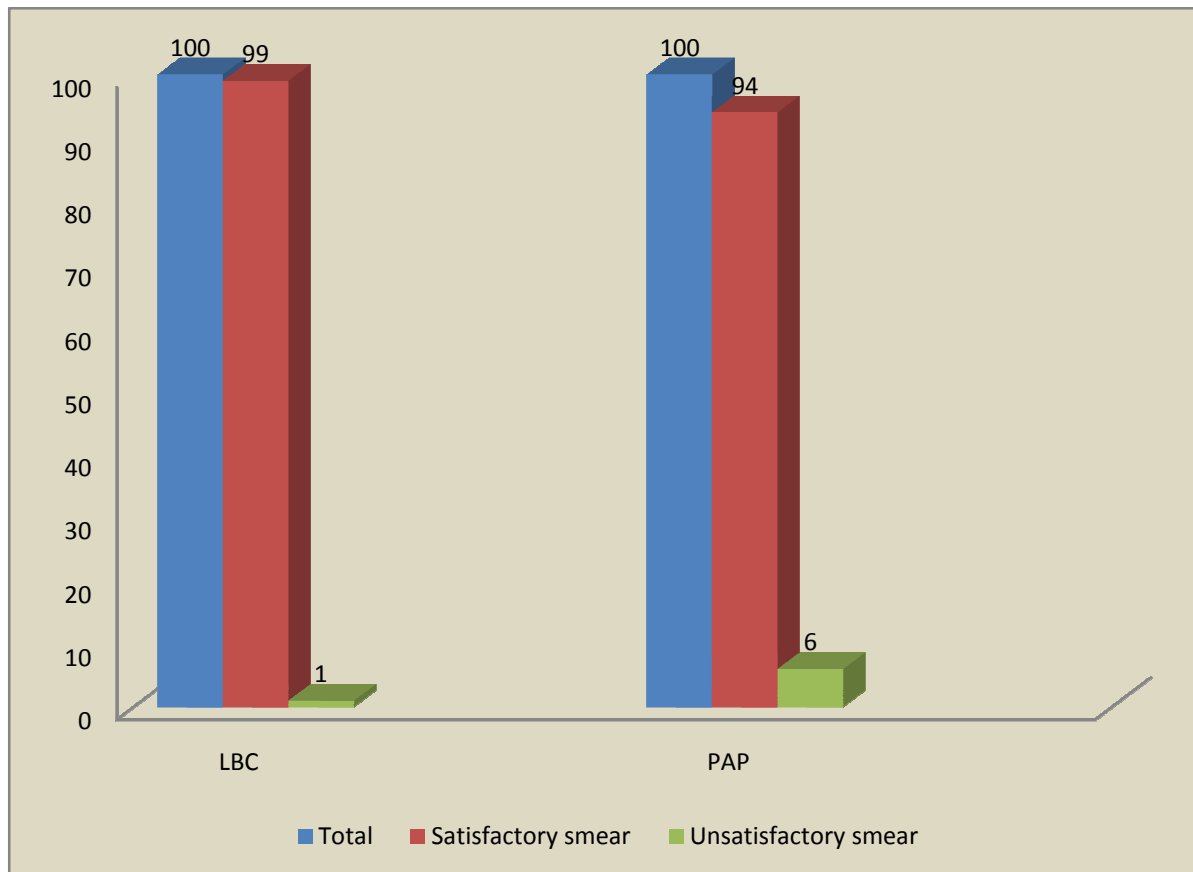


Table-15: Comparison of Infectious agent prediction in LBC and PAP

Infectious agent	LBC	PAP
Total cases	14	3
Bacterial Vaginosis	2	1
Candida	5	-
Trichomonas vaginalis	7	2

In the present study infectious agents were detected in 14 cases (14%) of LBC of these 2 cases showed features of Bacterial vaginosis , 5 cases showed features of Candida and TV in 7 cases.

Pap smear showed infectious agents in 3 cases (3%) of these 2 cases showed features of Trichomonas vaginalis and 1 case showed features of Bacterial vaginosis.

Figure 28: Comparison of Infectious agent prediction in LBC and PAP

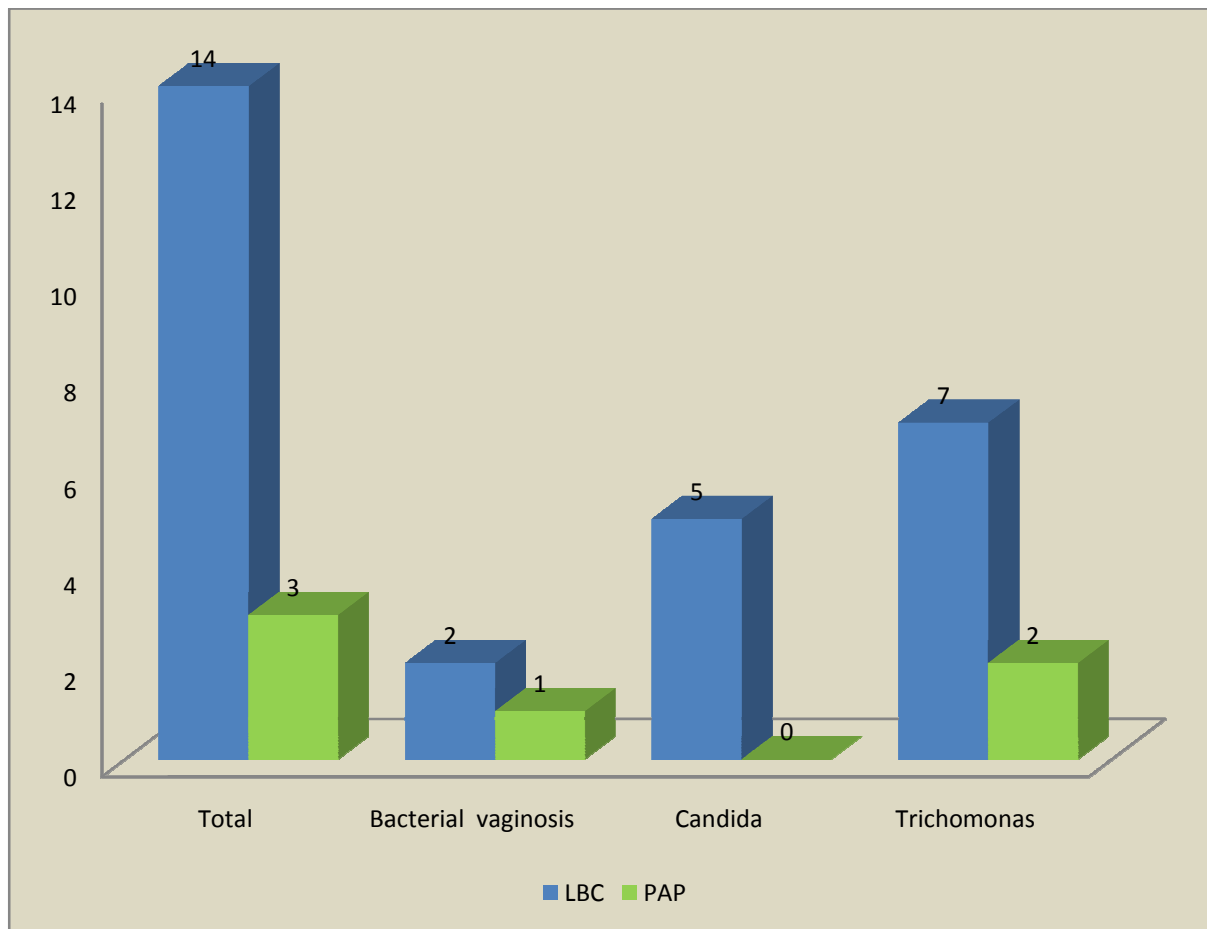


Table – 16: Distribution of cases in LBC

Bethesda category	LBC	Percentage
Normal	68	68
LSIL	16	16
HSIL	10	10
ASC(ASC-US&ASC-H)	2	2
SCC	4	4

In the present study out of 100 cases, LBC showed LSIL in 16 cases (16%), 10 cases (10%) showed features of HSIL. ASC was seen in 2 cases (2%) and Squamous cell carcinoma in 4 cases (4%).

Figure 29: Distribution of cases in LBC

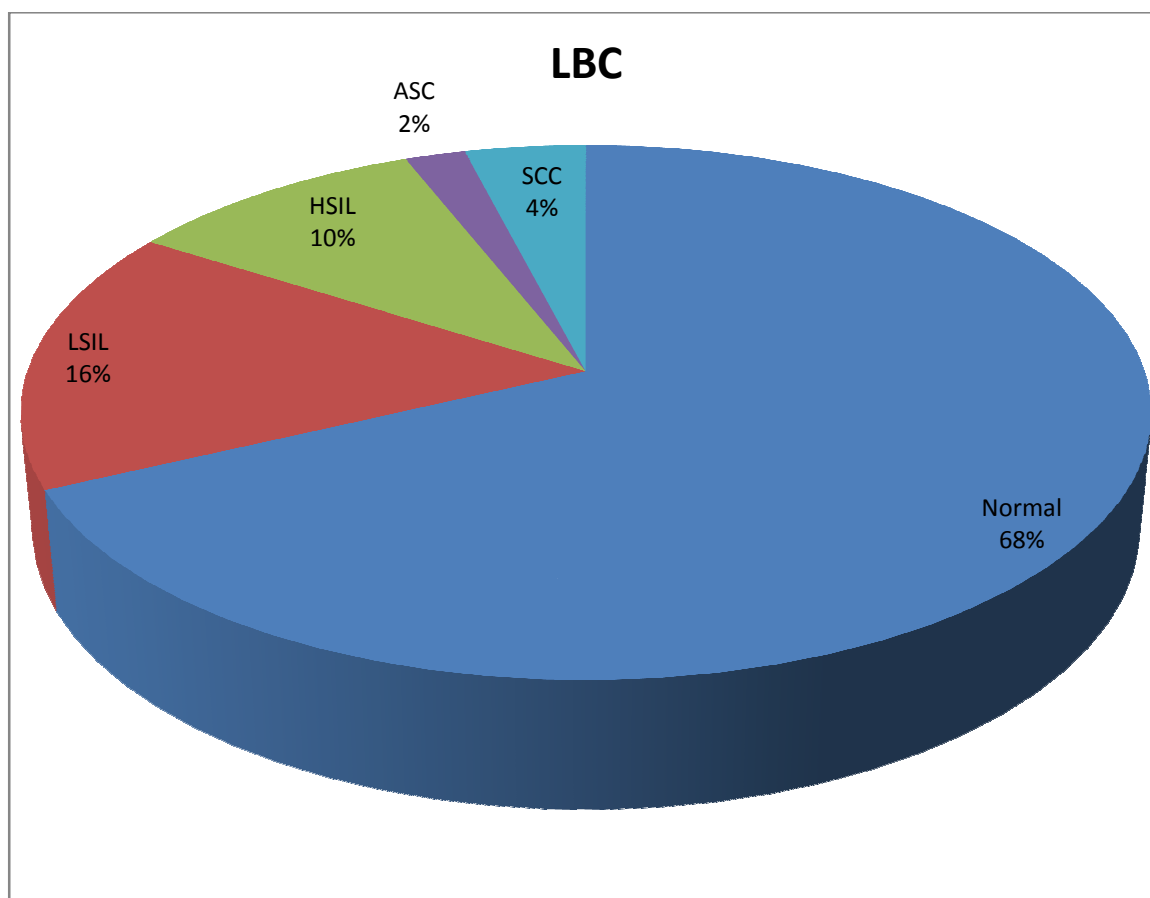


Table – 17: Distribution of cases in PAP

Bethesda category	PAP	Percentage
Normal	83	83
LSIL	5	5
HSIL	1	1
ASC(ASC-US&ASC-H)	8	8
SCC	3	3

Out of 100 cases, in Conventional Pap smear 5 cases(5%) showed LSIL, 1 case(1%) showed features of HSIL, ASC was seen in 8 cases(8%) , 3 cases (3%) showed features of Squamous cell carcinoma.

Figure 30: Distribution of cases in PAP

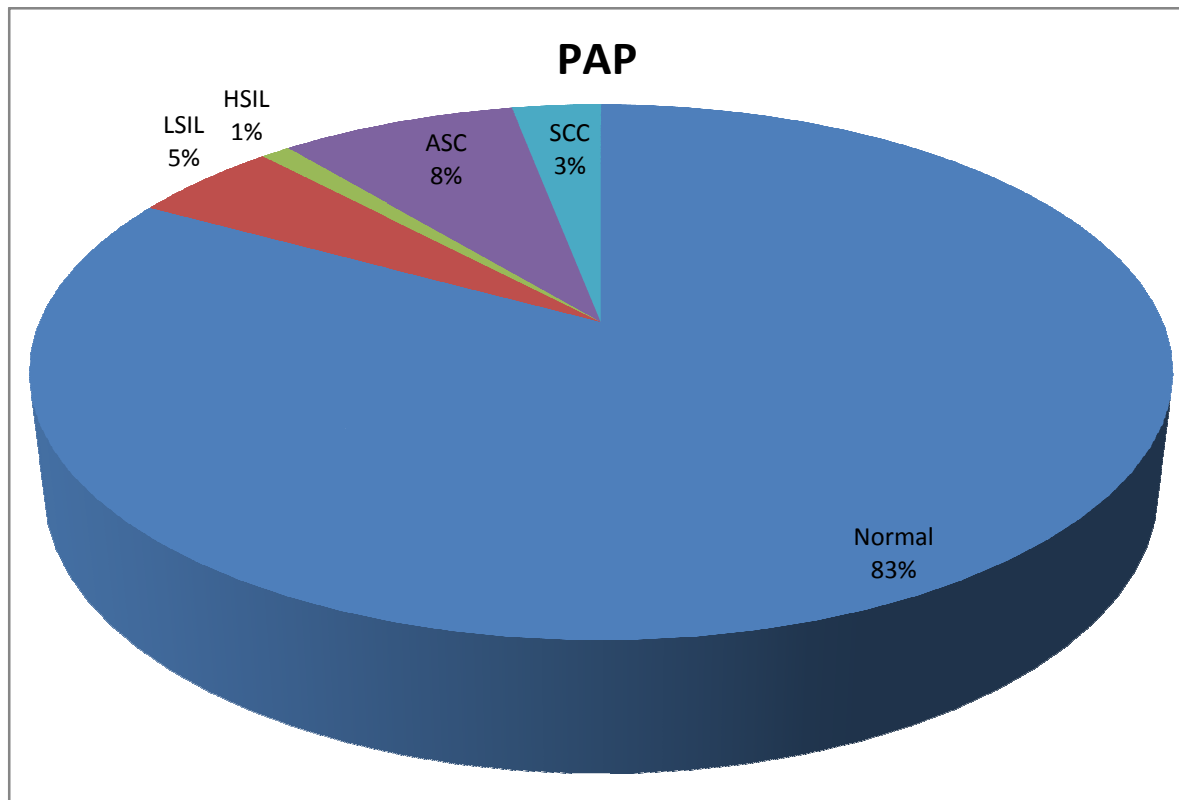


Table – 18: Comparison of Cytology abnormalities in LBC and PAP

Cytology		PAP				
LBC	Total	Normal	LSIL	HSIL	ASC	SCC
Normal	68	68	-	-	-	-
LSIL	16	8	5	-	3	-
HSIL	10	4	-	1	5	-
ASC	2	2	-	-	-	-
SCC	4	1	-	-	-	3

It is noted in the present study, all 68 normal cases in LBC showed normal reports in PAP. Out of 16 LSIL cases in LBC, 8 cases were normal in PAP, 5 cases showed LSIL and 3 cases showed ASC in PAP. Out of 10 HSIL cases in LBC, 4 were normal in PAP, 1 showed HSIL and 5 showed ASC. 2 ASC cases in LBC were normal in PAP. Out of 4 Squamous cell carcinoma in LBC, 3 cases showed Squamous cell carcinoma in PAP and 1 case was normal.

It is noted that LSIL and HSIL prediction was more with LBC which was statistically significant $p = 0.000$ and $p = 0.001$ respectively. ASC prediction was more with PAP which was statistically significant $p = 0.001$.

Figure 31: Comparison of Cytology abnormalities in LBC and PAP

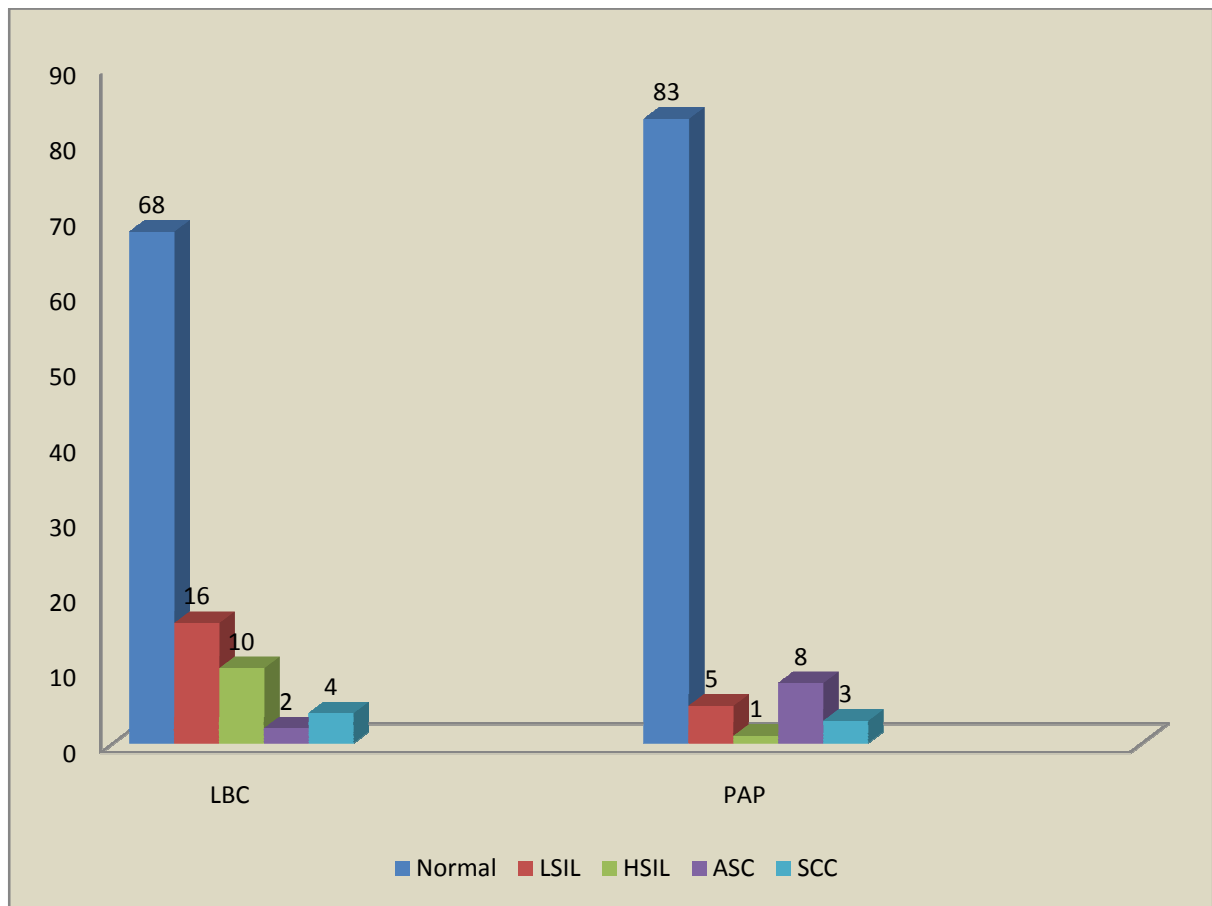


Table – 19: Distribution of cases by colposcopic findings

Colposcopy	Total cases	Percentage
Normal	66	66
LSIL	18	18
HSIL	12	12
Invasive Ca	4	4

In current study out of 100 cases, 66 (66%) cases showed normal findings in colposcopy, 18(18%) cases showed Low grade lesion, 12(12%) cases showed High grade lesion and 4 cases (4%) showed features of invasive carcinoma in colposcopy.

Table – 20: Comparison of Colposcopy, LBC, and PAP

Category	Colposcopy	LBC	PAP
Normal	66	68	83
LSIL	18	16	5
HSIL	12	10	1
Invasive Ca	4	4	3

In our study on comparing colposcopy with LBC and PAP, colposcopy was normal in 66 cases, in LBC it was 68 cases and in PAP smear 83 cases were normal. Colposcopy showed low grade lesion in 18 cases, LBC showed LSIL in 16 cases, and PAP showed LSIL in 5 cases .12 cases showed features of high grade lesion in colposcopy. LBC showed HSIL in 10 cases and PAP showed HSIL in 1 case. Colposcopy showed features of invasive cancer in 4 cases, in LBC it was 4 and in PAP it was 3.

Figure 32: Comparison of Colposcopy, LBC and PAP

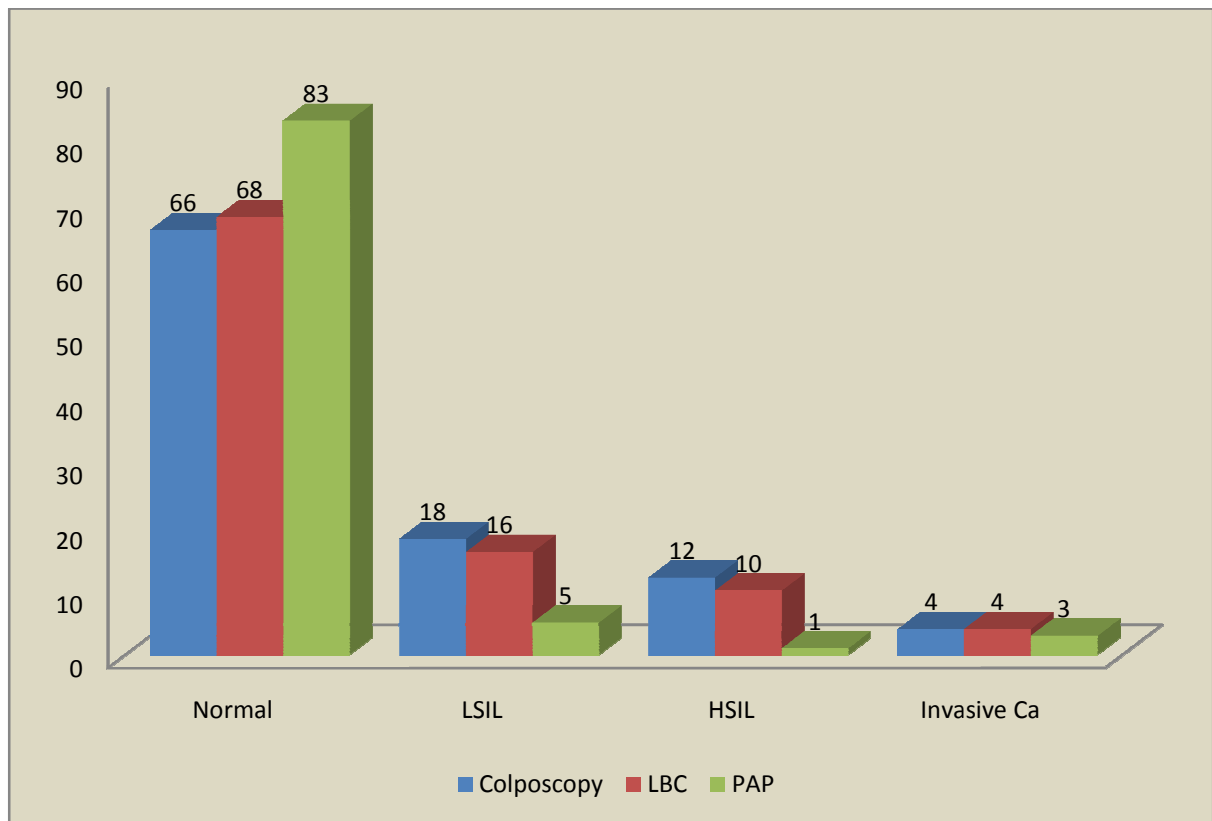


Table – 21: Distribution of cases by HPE findings

HPE	Total cases	Percentage
Normal	67	67
Abnormal	33	33
CIN 1	16	16
CIN 2	11	11
CIN 3	2	2
SCC	4	4

In the present study out of 100 cases, HPE showed abnormalities in 33(33%) cases of these 16 cases (16%) showed features of CIN 1, 11 cases (11%) showed CIN 2, and 2 cases (2%) showed CIN 3, 4 cases (4%) showed features of Squamous cell carcinoma.

Table – 22: Comparative study of Colposcopy and HPE

Colposcopy	HPE					Total
	Normal	CIN 1	CIN 2	CIN 3	SCC	
Normal	65	1	-	-	-	66
LSIL	2	16	-	-	-	18
HSIL	-	-	10	2	-	12
Invasive Ca	-	-	-	-	4	4
Total	67	17	10	2	4	100

In the present study on comparing colposcopy with HPE out of 66 normal cases in colposcopy 65 cases were normal in both HPE and colposcopy ,1 case showed CIN 1 in HPE. Of the 18 LSIL cases in colposcopy, 2 cases (12%) were normal in HPE and 16 cases (88%) showed CIN 1 .Out of 12 HSIL cases in colposcopy 10 cases (83%) showed CIN 2 and 2 cases (17%) showed CIN 3 in HPE. All the 4 cases of invasive cancer in colposcopy showed squamous cell carcinoma in HPE.

Table-23: Comparative study of LBC and HPE

CYTOLOGY	HPE					
LBC	Normal	CIN 1	CIN 2	CIN 3	SCC	Total
Normal	67	-	1	-	-	68
LSIL	-	12	4	-	-	16
HSIL	-	2	6	2	-	10
ASC	-	2	-	-	-	2
SCC	-	-	-	-	4	4
Total	67	16	11	2	4	100

It is noted in our study that out of 68 normal cases in LBC, 1 case showed features of CIN 2 on HPE and the remaining 67 cases were normal in both LBC and HPE. Out of 16 LSIL cases in LBC, 12 cases (75%) showed CIN 1 and 4 cases (25%) showed CIN 2 in HPE. Out of 10 HSIL cases in LBC, HPE showed CIN1 in 2 cases(20%),CIN 2 in 6 cases(60%) and CIN 3 in 2 cases(20%). 2 ASC cases in LBC showed features of CIN 1 in HPE. 4 Squamous cell carcinoma on LBC showed Squamous cell carcinoma on HPE.

It is noted that concordance between LBC abnormalities and HPE abnormalities were statistically significant p -0.000.

Figure 33: Comparative study of LBC and HPE

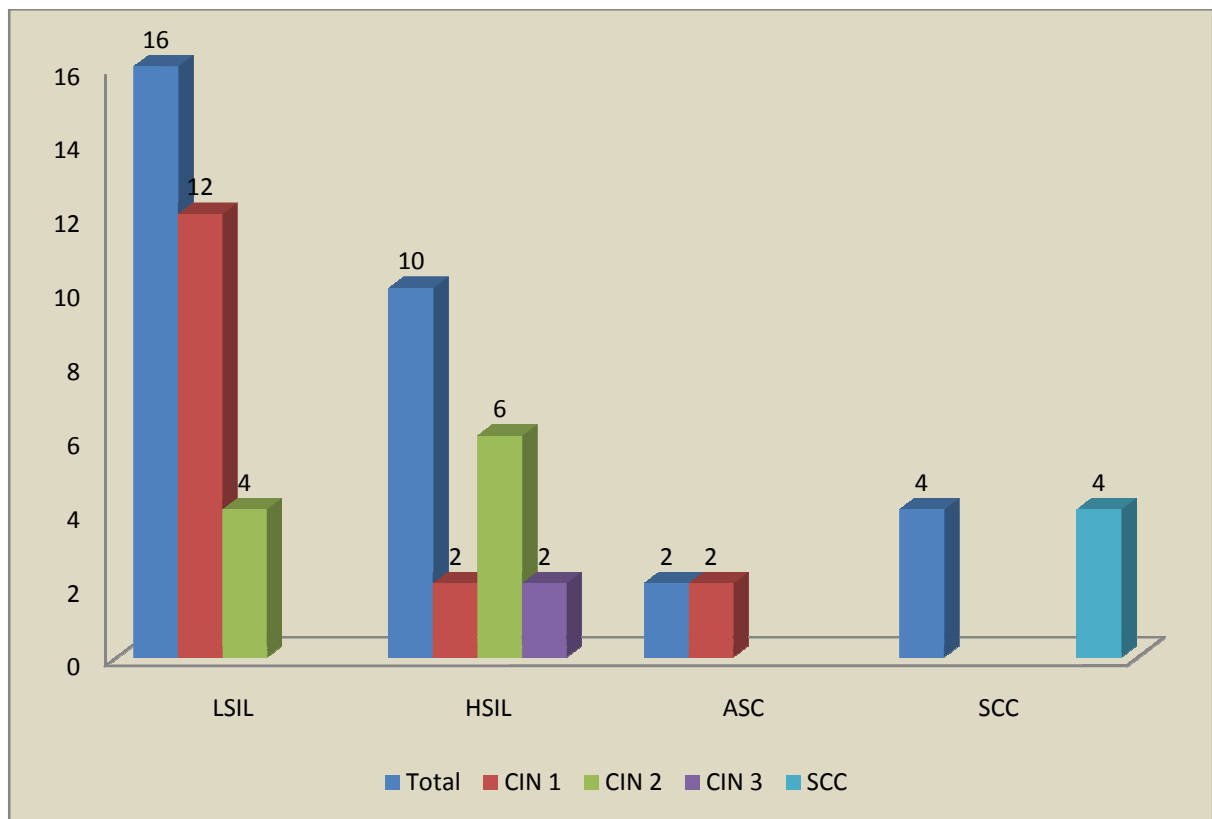


Table – 24: Comparative study of PAP and HPE

PAP	HPE					Total
	Normal	CIN 1	CIN 2	CIN 3	SCC	
Normal	67	10	5	-	1	83
LSIL	-	3	2	-	-	5
HSIL	-	-	-	1	-	1
ASC	-	3	4	1	-	8
SCC	-	-	-	-	3	3
Total	67	16	11	2	4	100

In the present study, it is noted that out of 83 normal cases in PAP, 67 cases were normal in both PAP and HPE. Of the remaining 16 normal cases in PAP, 10 cases showed CIN 1 in HPE, 5 cases showed CIN 2 in HPE, and 1 case showed features of Squamous cell carcinoma. PAP showed 5 LSIL cases, of which 3 cases (60%) showed CIN 1 and 2 cases (40%) showed CIN 2 on HPE. 1 HSIL case on PAP showed CIN 3 on HPE. Of the 8 ASC cases in PAP, 3 (38%) showed CIN 1, 4 (50%) showed CIN 2, and 1(12%) showed CIN 3 on HPE. All the 3 cases of Squamous cell carcinoma in PAP showed Squamous cell carcinoma in HPE.

In current study, concordance between PAP abnormalities and HPE abnormalities were statistically significant $p = 0.000$.

Figure 34: Comparative study of PAP and HPE

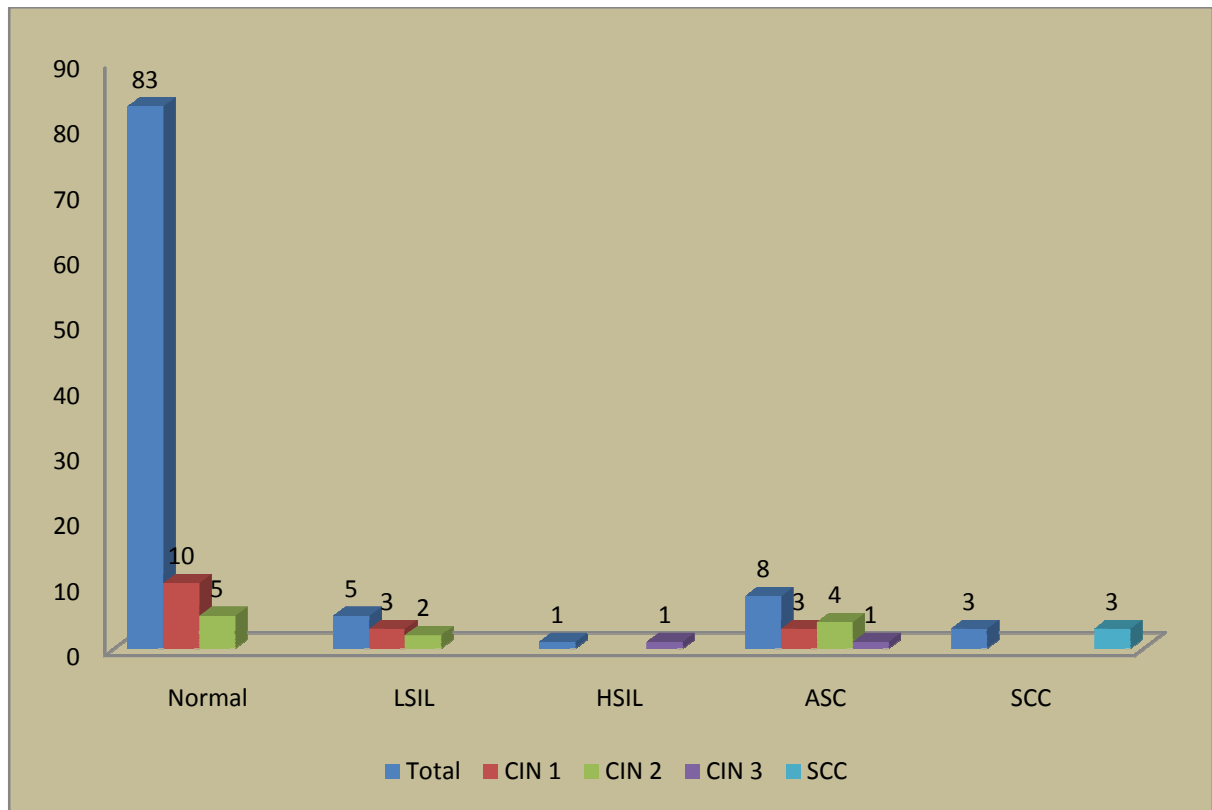


Table -25: LBC and HPE cross table – SENSITIVITY PREDICTION

LBC	HPE	
	Positive	Negative
Positive	32(true positive)	- (false positive)
Negative	1(false negative)	67 (true negative)

Sensitivity of LBC = $32 / 32 + 1 \times 100$

= 96 %

In the present study Sensitivity of LBC is 96%.

96 % sensitivity means 96% of the diseased people screened by LBC had true positive result and the remaining 4% had false negative result.

Specificity of LBC = $67 / 67 + 0 \times 100$

= 100 %.

In the present study specificity of LBC is 100 %.

Table-26: PAP and HPE cross tabulation - SENSITIVITY PREDICTION

PAP	HPE	
	Positive	Negative
Positive	17(true positive)	- (false positive)
Negative	16(false negative)	67(true negative)

Sensitivity of PAP = $17 / 16 + 17 \times 100$

$$= 51 \%$$

In our study sensitivity of PAP was found to be 51%.

51% of the diseased people screened by Pap test gave a true positive result and the remaining 49 % showed false negative report.

Specificity of PAP = $67 / 67 + 0 \times 100$

$$= 100 \%$$

In the present study specificity of PAP is 100 %.

Figure 35: Comparison of sensitivity and specificity in LBC and PAP

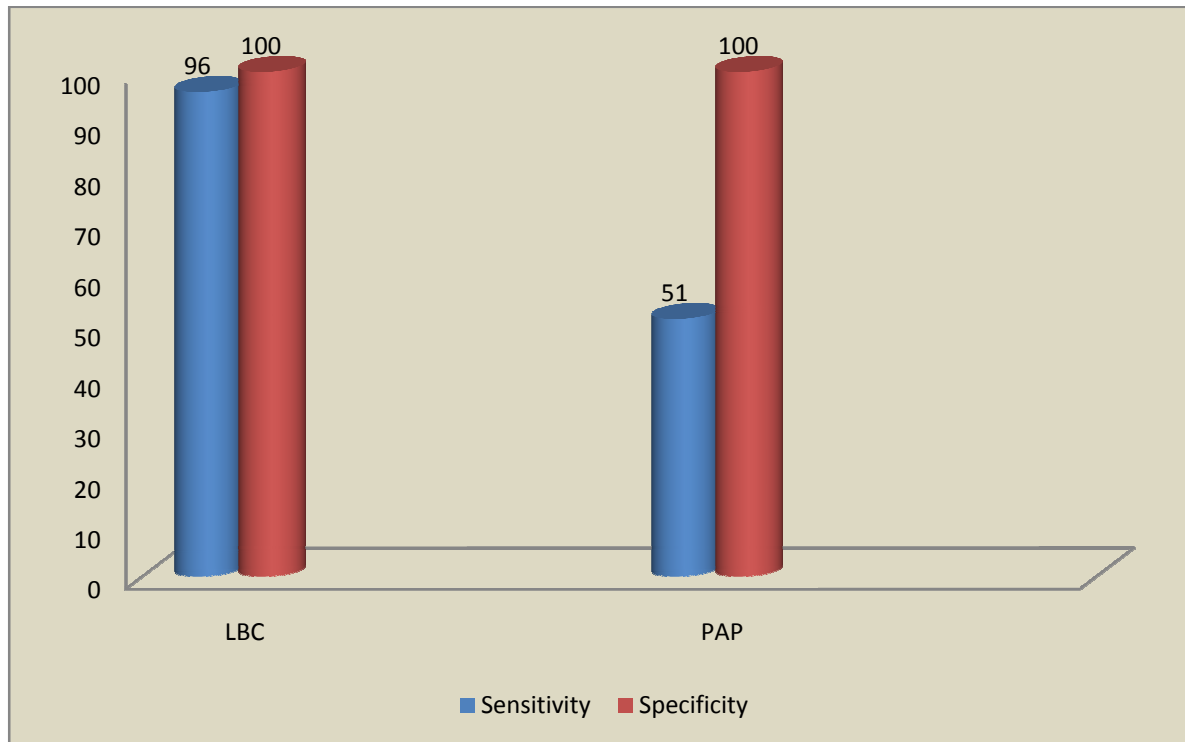


Table – 27: Comparison of Sensitivity and Specificity in LBC and PAP

Cytology	Sensitivity	Specificity
LBC	96%	100%
PAP	51%	100%

In our study, sensitivity of LBC screening test was 96 % and sensitivity of Pap test was 51 % .Specificity of both tests in our study was same that is 100%.

Discussion

DISCUSSION

Screening for cervical cancer has resulted in the reduction of incidence of cancer cervix and its complications. Pap smear has been used for the screening purpose since 1940's but studies have shown that the sensitivity of a single Pap test is low and it has high false negative rate. This is said to be due to improper sampling and ineffective interpretation. In Pap smear only 20% of the scraped cells in the Ayer's spatula are transferred to the slide while smearing, which is done manually. Therefore alternative screening methods which overcome these pitfalls in Pap smear is developed, one such method is Liquid Based Cytology where all the scraped cells in the cyto brush are transferred in the liquid transport medium to the laboratory where it is processed and a uniform thin layer of smear is prepared in the laboratory than manually. This study is done for evaluating the performance of Liquid Based Cytology and for doing comparative study of the sensitivity of LBC and the conventional Pap method.

The median age of cervical cancer diagnosis is in the mid to late forties approximately a decade later than CIN⁽¹⁶⁾. The cases of carcinoma cervix usually occur at 35 to 39 years and 60 to 64 years of age⁽⁵⁾. In the present study abnormal cases were mostly found in the fourth decade of life (table-6) and earliest age of occurrence of invasive squamous cell carcinoma was at 35 years, a finding similar to **Sherwani RK et al**⁽³⁷⁾ and in contrast to studies by **Parker et al**⁽⁵⁰⁾ in his studies cancer cervix cases were seen after 70 years of age.

Earlier age of occurrence of preinvasive cervical lesions and SCC were due to earlier age of marriage in our society.

In India women of low socio economic class and rural women showed higher incidence of cancer cervix (**Vallikad,Kurkure AP,Yeole BB**)^(39,40). The main explanation specified for this is lack of access to screening and health services and poor knowledge about the risk factors of cancer cervix.

In our study (table-7) 82% of abnormal cases were from Urban area in contrast to **Vallikad,Kurkure AP,Yeole BB**^(39,40). Our observation may be due to random case selection and most of our patients were from urban area.

In our study (table-8) 70 % of abnormal cases belonged to class IV socio economic class and 30 % belonged to class III socioeconomic class (Modified Kuppusamy scale), a finding similar to the study by **Sherwani RK etal**,⁽³⁷⁾**Christopherson and Parker**⁽⁴¹⁾ in their studies prevalence of cancer cervix cases were more in low socio economic class women with younger age of marriage and child bearing.

Immature squamous metaplasia with in the cervical transformation zone is the epithelium at risk for cellular transformation. The most active phase of metaplasia occurs during fetal life, in the years immediately following puberty and during first pregnancy⁽³⁶⁾.

In our study (table-9) 78% of cases with CIN and carcinomatous changes had onset of sexual activity at late second decade of life, a finding which correlates with the study of **Sherwani RK et al**⁽³⁷⁾ and **Rotkin**⁽⁴²⁾. Rotkin postulated that cancer cervix is transmitted through sexual intercourse from male to female, with a higher chance.

Data's from case – control studies indicate that high parity increases the risk of developing cervical cancer. Specifically women with seven prior full term pregnancies have an approximately four fold risk, and those with one or two have a twofold risk compared to nulliparous⁽⁴³⁾.

In our study 64 %(table-10) of the CIN and carcinoma cases had parity index of three or more concordant with **Sherwani RK et al**⁽³⁷⁾, **Shankaranarayana et al**⁽⁵¹⁾ and **Parker et al**⁽³⁸⁾.

The most common presenting complaint of abnormal cases in our study was discharge per vaginum 64 %, (table- 11) similar to **Sherwani RK et al**⁽³⁷⁾ and all the patients with post coital bleeding had CIN or carcinoma in our study. These results are consistent with the known association of cervical neoplasia with post coital bleeding (**Robert ME**)⁽⁴⁴⁾.

In our study 61% (table-12) of the cases with biopsy abnormality had clinically normal cervix and almost all patients with a clinically visible cervical lesion had either CIN or SCC.

Sherwani RK et al ⁽³⁷⁾ conducted a comparative study of Conventional Pap and liquid based cytology, where out of 160 cases cytological abnormality was found in 26.2% of cases by LBC and Pap smear showed abnormality in 15% of cases.

In the present study, LBC detected abnormality in 32% (table-13) of cases whereas Pap smear detected abnormality in 17% of cases, similar to the study by **Sherwani RK et al** ⁽³⁷⁾ and **Limaye et al** ⁽⁴⁵⁾ where SIL detection increased from 1.3% in Pap tests to 3.4% in LBC.

A reported advantage of LBC over Conventional Pap screening is the marked decrease in the number of unsatisfactory slides, and is related to the fact that 100% of the collected sample is transferred to the fluid vial and that the cell enrichment process reduces obscuring material such as blood, mucus and inflammatory cells.

Sylvia Taylor et al ⁽⁴⁶⁾ conducted a study and stated that treating unsatisfactory smear as negative did not change the sensitivity of LBC and the positive predictive value of LBC and Conventional Pap. In our study all unsatisfactory smears were considered as negative for intra epithelial lesions for comparative purposes.

In our study unsatisfactory smear for evaluation in LBC was 1% (table-14) compared to 6 % in Pap smear similar to the study by **Sherwani RK et al** ⁽³⁷⁾

and **Limaye et al** ⁽⁴⁵⁾. In the study conducted by **Sherwani RK et al** unsatisfactory smear on LBC was 3.7% and on Pap smear 5%; in **Limaye et al** study unsatisfactory specimen was 0.4% on LBC and 0.27% on Pap smear. Most of the unsatisfactory smear in Pap smear is due to thick smear and in LBC is due to scant cellularity a finding which correlates with the finding of **Diaz-Rosario, Kabawat** ⁽⁴⁷⁾ and **Sherwani RK et al** ⁽³⁷⁾.

In the present study infectious agents were detected in 14% of cases (table-15) on LBC and 3% of cases on Conventional Pap smear similar to the study by **Sherwani RK et al** ⁽³⁷⁾, where infectious agents are found in 8.7% of cases on LBC and 3.1% of cases on Pap smear.

In our study, the detection percentage of premalignant categories of LSIL and HSIL increased significantly for the LBC when compared to the Conventional smear, detection of LSIL increased from 5% to 16% with LBC (table -18) than with conventional Pap smear and detection of HSIL increased from 1% to 10% a finding which correlates with the finding of **Sherwani RK et al** ⁽³⁷⁾, **Limaye et al** ⁽⁴⁵⁾, **Diaz – Rosario and Kabawat** ⁽⁴⁷⁾.

Sherwani RK et al ⁽³⁷⁾ reported an increased percentage of cases of LSIL from 10.6% to 18% and HSIL from 0.6% to 4.3%. **Limaye et al** ⁽⁴⁵⁾ reported that detection of LSIL increased from 0.3% to 1% with LBC. **Diaz-Rosario and Kabawat** ⁽⁴⁷⁾ reported that LBC proportionally detected 71.65% and 102.5% more LSIL and HSIL cases respectively.

In a study conducted by **Zhu et al** ⁽²⁾ there was significantly reduced ASC, 8% with Pap smear to 4% with liquid based cytology. It is noted in our study that LBC showed 2% of ASC whereas Pap smear showed 8% of ASC similar to **Zhu et al** ⁽²⁾ .

In this study (table-18) the precision of the diagnosis of HSIL on PAP is significantly lower. Out of 10 (100%) HSIL cases in LBC, 10% showed HSIL, 50% showed ASC and 40 % showed normal study in PAP a finding similar to **Renshaw et al** ⁽⁴⁸⁾ .

Colposcopic guided biopsy was done in all 100 cases in our study of which (table-19) 34 cases showed colposcopic abnormality. On comparing colposcopic findings with LBC and Pap test (table-20) the accuracies of LBC and colposcopy, as methods of diagnosis of preclinical cervical cancer were very good in this study, and compared well to each other measured against histology as a gold standard. Colposcopy requires more sophisticated equipment and expertise in diagnosis than LBC. Hence LBC is a useful screening test for preinvasive cervical lesion.

In our study, on comparing colposcopy with HPE reports (table-22), 88% of low grade lesions on colposcopy showed CIN 1 on histology. Of the high grade lesions, 83% showed CIN 2 , 17% showed CIN 3 and 98% of colposcopic normal findings showed normal reports on histology similar to the

study by **Carta G et al** ⁽⁵²⁾ where a better concordance was shown between colposcopy and histology.

Sherwani RK et al ⁽³⁷⁾ reported in their study that out of 29 cases diagnosed as LSIL on LBC, 89.7 % cases had mild dysplasia, 6.9% each had normal histology and moderate dysplasia and out of the 7 cases of HSIL 14.3% had mild dysplasia and 85.7% cases had moderate dysplasia and all the 6 cases of squamous cell carcinoma on LBC revealed squamous cell carcinoma on histopathology. Similarly, in our study, out of 16 LSIL cases in LBC (table-23) 75% of cases showed CIN 1 and 25% of cases showed CIN 2 and 20% of HSIL cases showed CIN 1 and 80% showed CIN2 and CIN3, all 4 cases of squamous cell carcinoma on LBC showed squamous cell carcinoma on histology.

It is reasonable to infer from our biopsy correlation data that increase in the diagnosis of intra epithelial lesions by LBC method is not substantially due to an increased number of false positive results, which is similar to the study done by **Diaz-Rosario and Kabawat** ⁽⁴⁷⁾. The concordance between LBC abnormalities and HPE abnormalities were statistically significant ($p = 0.000$) in our study.

In the present study, on comparing PAP and HPE (table-24), 60% of LSIL cases showed CIN 1 and 1 HSIL case showed CIN 3 and 3 cases of squamous cell carcinoma showed the same in HPE, a finding similar to the study by **Sherwani RK et al** ⁽³⁷⁾.

Similar to **Sylvia Taylor et al** ⁽⁴⁶⁾ study, on comparing particular cytology and histology reports in our study, women with negative histology reports showed predominantly negative results in both LBC and Conventional PAP tests.

One of the components of the sensitivity level is the laboratory's ability to detect abnormal cells. The inability to detect these abnormal cells is best defined as false negative proportion. In our study, out of 83 normal cases in PAP, 10 cases showed CIN 1, 5 cases showed CIN 2 and 1 case showed SCC on HPE. Out of 68 normal cases in LBC 1 case showed CIN 2 on HPE hence the false negative rate for LBC (4%) was lower than the Conventional PAP (49%) similar to the study by **Beerman et al** ⁽⁴⁹⁾.

Though the specificity comparison is not included in the objective of our study it is inferred from our study that both LBC and PAP tests were equivalent in terms of specificity that is 100% similar to the study done by **Beerman et al** ⁽⁴⁹⁾, where specificity of LBC was 97.7% and PAP smear was 98.17%.

Table-28: Comparison of sensitivity of LBC and PAP (table-25, 26, 27)

Studies	LBC	PAP
Sherwani RK et al ⁽³⁷⁾	97.6%	53.7%
Bolick et al ⁽³²⁾	95.2%	85%
Beerman et al ⁽⁴⁹⁾	96.24%	92.04%
Karnon J et al ⁽⁵³⁾	80.1%	71.5%
Present study	96%	51%

It is noted in our study that sensitivity of LBC is better than PAP, similar to Sherwani RK et al ⁽³⁷⁾, Bolick et al ⁽³²⁾, Beerman et al ⁽⁴⁹⁾, and Karnon J et al ⁽⁵³⁾. In LBC the increased sensitivity is mainly due to better sample collection so that all the collected cells are transferred to the liquid medium and processed, the obscuring matters are eliminated, and an uniform thin layer of smear with even distribution of cells are produced, and in LBC accurate classification of abnormal cells as squamous intraepithelial lesion of either low grade or high grade is made. LBC had a greater decrease in false negative cases compared to PAP; from these findings it was made out that LBC is a better screening test than PAP tests.

Summary

SUMMARY

1. Conventional Pap smear and Liquid Based Cytology for Cervical Cancer

Screening – A Comparative Study was conducted during 12 months period from June 2011 to June 2012. Total 100 patients attending the outpatient Department of Gynaecology at CMCH were randomly studied.

2. It is noted that out of 100 cases 40% of cases belonged to fourth decade of life.

3. In our study 44% of abnormal cases belonged to fourth decade of life and the earliest age of occurrence of Squamous cell carcinoma was at 35 years.

4. It is noted that 82% of abnormal cases were from urban area and 18% from rural area.

5. In the present study 70% of abnormal cases belonged to socio economic class IV

6. In current study, 78% of abnormal cases started sexual activity at less than 20 years of age and no abnormality was detected in women who have started sexual activity after 26 years of age.

7. In the present study 64% of abnormal cases had parity index of 3 and above.

8. It is noted that 64% of abnormal cases presented with symptom of discharge P/V and 24% with post coital bleeding .All the cases with post coital bleeding had biopsy abnormality.

9. It is noted that 61% of abnormal cases had no clinically detectable lesion on cervix.
10. In our study LBC showed more abnormality (32% of cases) than Pap smear (17% of cases).
11. In our study unsatisfactory smear for evaluation was 6% in Pap smear and it was 1% in LBC.
12. In the present study infectious agent prediction was more with LBC (14%) than Pap smear (3%).
13. It is noted that LSIL (16%) and HSIL (10%) prediction was more with LBC than PAP smear (LSIL 5%, HSIL 1%) and it was statistically significant.
14. In our study on comparing LBC and PAP, ASC prediction was more with PAP (8%) than LBC (2%) and it was statistically significant.
15. In our study colposcopy detected abnormality in 34 % of cases. HPE detected abnormality in 33% of cases.
16. On comparing colposcopy and cytology the prediction of low grade and high grade lesions were similar for both LBC and colposcopy.
17. In the present study on comparing colposcopy and HPE, 88% of low grade lesions on colposcopy showed CIN 1 on HPE and 83% of high grade lesions on colposcopy showed CIN 2 on HPE.

18. In our study of the 16 LSIL cases in LBC 75% showed CIN 1 and 25% showed CIN 2.
19. In the present study of the 10 HSIL cases in LBC 60% showed CIN 2, 20% showed CIN 1 and CIN 3 respectively.
20. In this study of the 8 ASC cases in PAP, 50% of cases showed CIN 2, 38% of cases showed CIN 1, and 12% of cases showed CIN 3 on HPE.
21. In our study false negative rate of Pap smear (49%) was more than LBC (3%).
22. In our study both LBC and PAP showed 100 % specificity.
23. In the present study sensitivity of LBC was 96% and sensitivity of PAP was 51%.

Conclusion

CONCLUSION

1. In the present study Liquid Based Cytology is better than the Conventional Pap test in detection of preinvasive cervical lesions; this is mainly due to elimination of sampling error and decreasing the probability of false negative reports. The main aim of cervical screening test is detection of precancerous cervical lesions; it is obvious in this study Liquid Based Cytology certainly contributes to the achievement of this aim.
2. In our study on comparing Liquid Based Cytology method with Conventional Pap tests relative to histology, Sensitivity for the detection of cervical intraepithelial lesion with Conventional Pap smear was 51% and with Liquid Based Cytology it was 96%. There was 45% overall improvement in sensitivity with Liquid Based Cytology. The increased sensitivity of LBC is from increased detection of cytologic abnormality.
3. It is inferred from our findings that Liquid Based Cytology is a superior screening test compared to Conventional Pap test.

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Annexure

PROFORMA

Name:

SE class:

Age :

Parity index:

O.P number:

Address:

Rural / Urban:

COMPLAINTS

HISTORY OF PRESENT ILLNESS

PAST HISTORY

PERSONAL HISTORY

MENSTURAL HISTORY

MARITAL HISTORY

OBSTETRIC HISTORY

General Examination

Systemic Examination

Per abdominal Examination

Per speculum Examination

Per vaginal examination

INVESTIGATIONS

LBC results

PAP results

Colposcopy results

HPE results

ஒப்புதல் படிவம் (CONSENT FORM)

நான் கர்ப்பப்பையின் வாயில் சதை எடுத்து பரிசோதனை செய்து கொள்ள முழுமனதுடன் சம்மதம் தெரிவித்துக் கொள்கிறேன். மேலும் இப்பரிசோதனையின் மூலம் கர்ப்பப்பையின் வாயில் பாதிப்பு உள்ளதா என்பதை அறிய முடியும் என்று மருத்துவர் மூலம் அறிந்துகொண்டேன்.

இப்படிக்கு

Key to Masterchart

KEY TO MASTER CHART

ASC – H	Atypical Squamous Cell cannot exclude High grade lesion
ASC – US	Atypical Squamous Cell of Undetermined significance
BV	Bacterial vaginosis
Ca	Cancer
CIN	Cervical Intraepithelial Lesion
Cx	Cervix
HPE	Histo Pathologic Examination
HSIL	High Grade Squamous Intraepithelial Lesion
L	Living
LSIL	Low Grade Squamous Intraepithelial Lesion
LBC	Liquid Based Cytology
N	Normal
P	Para
PAP	Papanicolaou test
P /S	Per speculum
P/V	Per vaginal
SCC	Squamous Cell Carcinoma
SE	Socio Economic
TV	Trichomonas vaginalis

Masterchart

S. No	OP No	Name of the Patient	Age (Yrs)	Place	SE Class	Age at First coitus(yrs)	Parity Index	Symptoms	P/S Examn	LBC	PAP	Colposcopy	HPE
1	19516	Shanthi	33	Rural	IV	25	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N
2	22060	Jothilakshmi	38	Rural	IV	19	P ₄ L ₄	Lower Abdomen Pain	Erosion Cx	LSIL	ASC-US	LSIL	CIN1
3	185409	Salyammal	40	Urban	IV	20	P ₂ L ₂	Discharge PV	N	TV	TV	N	N
4	185010	Kanagamani	42	Rural	IV	23	P ₃ L ₂	Postcoital bleed	Erosion Cx	HSIL	N	HSIL	CIN2
5	101123	Jagadeswari	47	Rural	IV	22	P ₂ L ₂	Discharge PV	N	Candida	N	N	N
6	148526	Shanthikandan	29	Urban	II	20	P ₁ L ₁	Lower Abdomen Pain	N	N	N	N	N
7	186517	Saranya	21	Urban	III	17	P ₂ L ₂	Discharge PV	N	TV	Unsatisfactory	N	N
8	184944	Revathi	25	Urban	IV	19	P ₂ L ₂	Discharge PV	N	N	N	N	N
9	190685	Lakshmi	43	Urban	III	21	P ₄ L ₄	Postcoital bleed	Eversion Cx	HSIL	ASC-US	HSIL	CIN2
10	190910	Jayalakshmi	35	Rural	IV	22	P ₂ L ₂	Discharge PV	N	N	N	N	N
11	155418	Vasanthi	25	Urban	IV	19	P ₂ L ₂	Discharge PV	N	LSIL	ASC-US	HSIL	CIN2
12	191010	Saraswathi	35	Rural	IV	25	P ₂ L ₂	Discharge PV	N	N	N	N	N
13	190423	Saraswathi	38	Urban	III	20	P ₂ L ₂	Discharge PV	N	LSIL	N	LSIL	CIN1
14	197603	Kuppammal	28	Urban	IV	22	P ₂ L ₂	Discharge PV	N	N	N	N	N
15	197932	Balkish	32	Urban	III	18	P ₃ L ₃	Discharge PV	Erosion Cx	LSIL	LSIL	LSIL	CIN1
16	84805	Revathi	23	Rural	IV	20	P ₁ L ₁	Discharge PV	N	N	N	N	N
17	203708	Renuka	30	Urban	IV	20	P ₃ L ₃	Discharge PV	N	N	N	N	N
18	84895	Devi	26	Rural	IV	22	P ₂ L ₂	Discharge PV	N	N	N	N	N
19	204807	Govindammal	35	Urban	IV	30	P ₁ L ₁	Discharge PV	N	N	N	N	N
20	208541	Sasikala	31	Urban	III	19	P ₂ L ₁	LowerAbdomenPain	N	N	N	N	N
21	209516	Kavitha	25	Urban	III	17	P ₄ L ₃	Discharge PV	Eversion Cx	LSIL	LSIL	LSIL	CIN1
22	208956	Shanthi	23	Urban	IV	19	P ₂ L ₂	Discharge PV	N	N	N	N	N
23	204167	Rosy	39	Urban	III	22	P ₃ L ₃	Discharge PV	N	N	N	N	N
24	214821	Anjalidevi	45	Rural	IV	25	P ₄ L ₄	Discharge PV	Ulcer Cx	SCC	SCC	invasive Ca	SCC
25	210712	Hameeda	35	Rural	IV	27	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N

S. No	OP No	Name of the Patient	Age (Yrs)	Place	SE Class	Age at First coitus(yrs)	Parity Index	Symptoms	P/S Examn	LBC	PAP	Colposcopy	HPE
26	214797	Seetha	36	Urban	III	24	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N
27	214595	Sulochana	35	Urban	IV	23	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N
28	181351	Revathi	32	Urban	III	21	P ₂ L ₂	Discharge PV	N	N	N	N	N
29	36388	Anitha	34	Rural	IV	24	P ₂ L ₂	Discharge PV	N	TV	TV	N	N
30	218651	Eswari	29	Urban	IV	21	P ₂ L ₂	Discharge PV	N	N	N	N	N
31	219505	Nathiya	26	Rural	IV	21	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N
32	93230	Sumithra	32	Urban	IV	20	P ₂ L ₂	Discharge PV	N	N	N	N	N
33	220272	Rabiya	34	Urban	IV	19	P ₃ L ₃	Discharge PV	Hypertrophy Cx	LSIL	N	LSIL	CIN1
34	219183	Venkatammal	40	Urban	IV	23	P ₂ L ₂	Discharge PV	N	N	N	N	N
35	224451	Chinthamani	42	Rural	IV	17	P ₃ L ₃	Discharge PV	N	N	N	N	N
36	224867	Shanthi	42	Urban	III	30	P ₁ L ₁	Lower Abdomen Pain	N	N	N	N	N
37	224881	Manju	32	Urban	IV	21	P ₂ L ₂	AUB	N	BV	Unsatisfactory	N	N
38	224582	Ramlath	24	Rural	IV	19	P ₂ L ₂	Discharge PV	N	N	N	N	N
39	225254	Chandra	35	Urban	IV	23	P ₂ L ₂	Discharge PV	N	LSIL	ASC-US	LSIL	CIN1
40	228486	Vijaya	30	Urban	IV	24	P ₂ L ₂	AUB	N	Candida	N	N	N
41	234584	Sivakami	45	Urban	IV	19	P ₃ L ₃	Discharge PV	N	LSIL	LSIL	LSIL	CIN1
42	234213	Sutha	24	Urban	III	20	P ₂ L ₂	Discharge PV	N	N	N	N	N
43	240169	Nagaselvi	45	Urban	III	21	P ₃ L ₃	Discharge PV	N	LSIL	N	LSIL	CIN1
44	239978	Jaya	31	Urban	III	25	P ₂ L ₂	Discharge PV	N	N	N	N	N
45	240252	Poongodi	26	Urban	IV	20	P ₂ L ₂	Discharge PV	N	N	N	N	N
46	94192	Kavitha	35	Urban	IV	20	P ₃ L ₃	Discharge PV	N	HSIL	N	LSIL	CIN1
47	252239	Chitra	28	Urban	III	21	P ₂ L ₂	Discharge PV	N	N	N	N	N
48	258167	Malar	28	Urban	IV	20	P ₂ L ₂	AUB	N	N	N	N	N
49	258316	Jansimary	23	Rural	IV	21	P ₁ L ₁	AUB	N	N	N	N	N
50	284196	Dhanalakshmi	36	Urban	III	20	P ₃ L ₃	Discharge PV	N	LSIL	N	LSIL	CIN1

S. No	OP No	Name of the Patient	Age (Yrs)	Place	SE Class	Age at First coitus(yrs)	Parity Index	Symptoms	P/S Examn	LBC	PAP	Colposcopy	HPE
51	308173	Saroja	55	Rural	IV	18	P ₃ L ₃	Discharge PV	N	N	N	N	N
52	308751	Rukmani	45	Rural	III	23	P ₂ L ₂	Lower Abdomen Pain	N	LSIL	N	LSIL	CIN1
53	427214	Janaki	33	Urban	III	24	P ₂ L ₂	Discharge PV	N	N	N	N	N
54	432641	Jothimani	42	Urban	IV	21	P ₁ L ₁	Discharge PV	N	N	N	N	N
55	321950	Lakshmi	55	Urban	IV	17	P ₅ L ₅	Discharge PV	N	ASC-US	N	LSIL	CIN1
56	325956	Rabiya	28	Urban	III	19	P ₃ L ₃	Discharge PV	N	HSIL	N	HSIL	CIN2
57	273491	Bhuvaneswari	33	Rural	IV	22	P ₂ L ₂	Discharge PV	N	Candida	Unsatisfactory	LSIL	N
58	331907	Deepa Bharathi	27	Urban	IV	24	P ₁ L ₁	Lower Abdomen Pain	N	N	N	N	N
59	332154	Udaya	36	Urban	IV	21	P ₂ L ₂	Postcoital bleed	N	HSIL	N	HSIL	CIN2
60	320085	Maheswari	32	Urban	III	25	P ₂ L ₂	AUB	N	N	N	N	N
61	333162	Kala	34	Urban	IV	21	P ₁ L ₁	Lower Abdomen Pain	N	N	N	N	N
62	338540	Backiyam	31	Urban	III	24	P ₁ L ₁	AUB	N	N	N	N	N
63	338840	Amutha	42	Urban	IV	17	P ₄ L ₄	Postcoital bleed	UlcerCx	HSIL	ASC-H	HSIL	CIN2
64	343479	Manjula	23	Rural	IV	17	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N
65	343902	Thangammal	55	Urban	IV	19	P ₃ L ₃	Discharge PV	N	LSIL	LSIL	LSIL	CIN2
66	343972	Vasanthi	34	Urban	IV	24	P ₂ L ₂	Discharge PV	N	TV	N	N	N
67	348633	Karpagavalli	28	Urban	IV	20	P ₂ L ₂	Lower Abdomen Pain	N	TV	N	N	N
68	329401	Sivakami	55	Urban	IV	22	P ₂ L ₂	Discharge PV	N	LSIL	LSIL	HSIL	CIN2
69	348651	Gomathi	24	Urban	IV	21	P ₁ L ₁	Discharge PV	N	N	N	N	N
70	329139	Kamalan	52	Urban	IV	22	P ₂ L ₂	Discharge PV	N	Unsatisfactory	Candida	N	N
71	362336	Saraswathi	51	Urban	III	18	P ₅ L ₅	Postcoital bleed	Papillary Cx	HSIL	ASC-US	HSIL	CIN3
72	368021	Thangam	35	Urban	IV	17	P ₃ L ₃	Postcoital bleed	Ulcer Cx	SCC	SCC	invasive Ca	SCC
73	362961	Sasireka	30	Urban	III	20	P ₂ L ₂	Discharge PV	N	BV	Unsatisfactory	LSIL	N
74	363328	Sakunthala	21	Urban	IV	17	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N
75	363161	Sutha	22	Urban	III	19	P ₁ L ₁	Discharge PV	N	N	N	N	N

S. No	OP No	Name of the Patient	Age (Yrs)	Place	SE Class	Age at First coitus(yrs)	Parity Index	Symptoms	P/S Examn	LBC	PAP	Colposcopy	HPE
76	363814	Sumithra	29	Rural	IV	21	P ₂ L ₂	Discharge PV	N	N	N	N	N
77	363882	Radha	30	Urban	IV	20	P ₂ L ₂	Discharge PV	N	TV	N	N	N
78	364213	Suja	44	Urban	IV	23	P ₂ L ₂	Discharge PV	N	N	N	N	N
79	363991	Manimegalai	45	Urban	IV	22	P ₃ L ₂	Discharge PV	N	LSIL	N	HSIL	CIN2
80	364000	Kalarani	24	Urban	IV	21	P ₁ L ₁	Discharge PV	N	N	N	N	N
81	364803	Umamaheswari	29	Urban	IV	22	P ₂ L ₂	Discharge PV	N	N	N	N	N
82	364875	Bhuvaneswari	31	Rural	IV	23	P ₁ L ₁	Discharge PV	N	N	N	N	N
83	359647	Chitra	30	Urban	IV	19	P ₂ L ₂	Lower Abdomen Pain	N	ASC-US	N	LSIL	CIN1
84	360005	Sasikala	32	Urban	III	22	P ₂ L ₂	Discharge PV	N	N	N	N	N
85	359887	Vijayalakshmi	36	Urban	IV	24	P ₂ L ₂	Discharge PV	N	N	N	N	N
86	360186	Sundari	50	Urban	III	22	P ₂ L ₂	Lower Abdomen Pain	N	N	N	N	N
87	49633	Rajammal	40	Urban	IV	20	P ₄ L ₄	Discharge PV	N	HSIL	ASC-H	HSIL	CIN2
88	380471	Vasantha	42	Urban	III	23	P ₁ L ₁	Discharge PV	N	N	N	N	N
89	380592	Dhanalakshmi	40	Urban	IV	19	P ₃ L ₃	Discharge PV	N	HSIL	HSIL	HSIL	CIN3
90	396662	Chellamma	35	Urban	IV	22	P ₂ L ₂	Discharge PV	N	LSIL	N	LSIL	CIN1
91	365179	Maragatham	33	Rural	IV	21	P ₃ L ₃	Lower Abdomen Pain	N	N	N	N	N
92	526481	Mani	55	Urban	IV	20	P ₅ L ₅	Discharge PV	Hypertrophy Cx	HSIL	ASC-US	LSIL	CIN1
93	48691	Parameswari	45	Urban	IV	23	P ₃ L ₃	Discharge PV	N	Candida	N	N	N
94	397962	Rathinam	39	Urban	III	20	P ₂ L ₂	Discharge PV	N	LSIL	N	N	CIN1
95	401927	Saraswathi	47	Rural	IV	20	P ₃ L ₃	Postcoital bleed	Papillary Cx	SCC	SCC	invasive Ca	SCC
96	415809	Vijayarani	55	Urban	IV	20	P ₄ L ₄	Postcoital bleed	Ulcer Cx	SCC	Unsatisfactory	invasive Ca	SCC
97	423694	Sumithra	29	Urban	IV	21	P ₂ L ₂	Discharge PV	N	N	N	N	N
98	432406	Resitha	30	Urban	III	22	P ₁ L ₁	Lower Abdomen Pain	N	N	N	N	N
99	349219	Padma	29	Urban	III	20	P ₂ L ₂	Discharge PV	N	N	N	N	N
100	421945	Susila	39	Rural	IV	20	P ₁ L ₁	Lower Abdomen Pain	N	TV	Unsatisfactory	HSIL	CIN2